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THE SHATTUCK LECTURE

MEDICAL EDUCATION AND THE PHYSICIAN*

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ALTHOUGH medical education has always been a central interest of the Massachusetts Medical Society, it has never before been the subject of a Shattuck lecture. It seems, therefore, to be an appropriate occasion to consider the role that organized medicine, as represented by the Society, has played and is playing in the advancement of medical education. I shall limit my attention to the undergraduate phase of the education of a physician and shall comment on some recent trends.

EXTERNAL INFLUENCES

Massachusetts furnishes a good example of the evolution of medical education in the country at large. The earliest settlers had no physicians among them but depended usually on the clergyman to minister to their physical as well as to their spiritual ills. Later, physicians trained by the apprentice system in England migrated to these shores and established apprenticeships of their own. A few among them held degrees from British schools, but throughout the eighteenth and well into the nineteenth century the vast majority of physicians were trained entirely under the apprentice system.

Under this system the practicing physician bore the complete educational responsibility that has now devolved on faculties of medicine. Each doctor who trained apprentices was, in effect, an independent peripatetic medical school. He handed down the lore he had himself accumulated and no doubt garnished it with some required reading in whatever medical classics were at hand.

An outstanding example of the practitioner as medical educator is seen in the career of Dr. Edward Augustus Holyoke, of Salem. After graduating from Harvard College in 1746, he apprenticed himself to Dr. Berry, of Ipswich, with whom he studied for two years. He then settled in Salem, where he practiced for the rest of his life, which proved to be a long one. He died in his one hundred and first year, having led an active professional life of nearly eighty years, during which he had been a preceptor to no less than 35 medical students. Dr. Holyoke was one of the original incorporators of the Massachusetts Medical Society and its first president. He was the first person to be awarded an honorary M.D. degree from Harvard (in 1783), and who can say that it was not well earned?

It was a desire for professional self-improvement that brought together a number of these worthy practitioners in the organization of the Massachusetts Medical Society in 1781. This is indicated by a letter to the public in the handwriting of John Warren, which refers to the organization of the Society:

> The design of the above institution is to promote medical and surgical knowledge . . . as well as to make a just discrimination between such as are duly educated and properly qualified for the duties thereof, and those who may ignorantly and wickedly administer medicine, whereby the health and lives of many valuable citizens may be endangered and perhaps lost to the community.

It is apparent that the founding fathers believed that standards of medical education were inseparably bound up with quality of medical practice and that neither could flourish without the other.

In the original bill of incorporation, the president and fellows of the Massachusetts Medical Society were authorized to examine all "Candidates for the Practice of Physic and Surgery" and to issue to those who were found qualified "Letters Testimonial of such Examination, under the Seal of said Society." These "Letters Testimonial" were, in effect, licenses to practice.

In accordance with a pattern that is now familiar the Society gradually raised its minimum requirements for licensure. In the beginning a candidate for examination need only have studied for "three full years" under the direction of "some respectable physician." He was examined by the censors in only three subjects—physiology, pathology and therapeutics.

It is an interesting side light that the Harvard Medical School and the Massachusetts Medical Society got under way in the same year, 1782, although the So-

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ciety had been incorporated in the previous year. Almost immediately arose the question whether the right to license practitioners that had been granted to the Society by the legislature was an exclusive right. After repeated conferences between the officers of the Society and the Corporation of Harvard College it was settled that a diploma from the University would be equivalent to "Letters Testimonial" from the Society.[1] Harvard was the third medical school to be organized in the United States, having been preceded by Pennsylvania and King's College (which later became the College of Physicians and Surgeons of Columbia University). These early schools were designed as supplements to the apprentice method of instruction and not as substitutes for it, and for that reason the courses of instruction were brief and concentrated. The standard school year was four months.[2] In 1789, backed by a special act of the legislature empowering the Society to prescribe the medical instruction or education that it judged requisite for admission to the examination of the Society, the Council considered the following resolution:

> Resolved, That in order to entitle any candidate to an examination before the Censors of this Society, it is requisite that in addition to an accurate knowledge of the English language he be able to construe & translate both Latin & Greek & have been instructed in the rudiments of Natural Philosophy, certificates of which to be produced to the satisfaction of the Censors—he will also bring a certificate that in addition to such education he hath studied three full years with some practitioner or practitioners of Physic & Surgery and attended on his or their practice; during which time he hath read the most approved authors in Anatomy, Physiology, Chemistry, Materia Medica, Surgery & Theory & Practice of Physic; provided, nevertheless, that any candidate who hath had the benefit of an education at some college or university, shall be entitled to an examination after having studied two full years with a practitioner or practitioners as aforesaid. The Society, impressed with a sense of the great importance of a college or university education do recommend it accordingly — also a knowledge of the French language & an attendance upon at least one course of actual anatomical dissections.

This report was adopted with minor amendments in the following year.[1] It would be of interest to know how many members of the Massachusetts Medical Society could qualify for such an examination today; I daresay that not more than two or three could "construe and translate both Latin and Greek."

Looking back on this report of the Council, one cannot but take pride in discerning there, in the womb of the Society, the primitive anlage of the structure of medical education as it exists today. One notes at the same time the concern of organized medicine for setting and enforcing standards of practice and its recognition of the contribution that universities had to offer.

In 1806 a knowledge of the principles of geometry and experimental philosophy were added to the requirements for certification by the Society. Greek was later dropped, and in 1850 the regulations were revised to require "two full courses on anatomy, physiology, chemistry, materia medica, midwifery, and the theory and practice of medicine and surgery."[1]

As time went on, the requirement of three years of practice under supervision was eliminated, and graduation from an approved medical school substituted. Up to 1922 the Council of the Massachusetts Medical Society maintained its own list of approved medical colleges, a function now carried on by the Council on Medical Education and Hospitals of the American Medical Association.

This brings me to a consideration of the part that the American Medical Association in turn has played in the improvement of medical education in the United States, for the national organization has to a large extent centralized activities in this sphere that had formerly been carried on by the state societies. The first step toward the formation of the American Medical Association was the introduction of a resolution by Dr. Nathan Smith Davis at a meeting of the Medical Society of the State of New York in 1845.[2] This resolution begins as follows:

> *Whereas,* It is believed that a national convention would be conducive to the elevation of the standard of medical education in the United States, and
>
> *Whereas,* There is no mode of accomplishing so desirable an object without concert of action on the part of the medical colleges, societies, and institutions of all the states, therefore, be it
>
> *Resolved,* That the New York State Medical Society earnestly recommends a national convention of delegates from medical societies and colleges in the whole Union to convene in the City of New York on the first Tuesday in May in the year 1846 for the purpose of adopting some concerted action on the subject in the foregoing preamble.

This resolution, having been adopted, led directly to an organizational meeting in the following year and to the formation of the American Medical Association. It is noteworthy that medical education ranked as the primary concern of the founders of the American Medical Association and that representatives of medical colleges participated at this first meeting.

The next fifty years witnessed the spanning of the continent by railroads and the great migration to the West. It was a period of rapid population growth, with corresponding demands for physicians without too many questions asked about their training. In this lush soil a rank assortment of good and bad schools flourished, giving, or pretending to give, some sort of medical education. There were cultist schools such as the homeopathic and the naturopathic; there were out-and-out diploma mills; there were commercial schools, operated for a profit, and there were university-connected medical schools. Even the last had rather tenuous connections with their parent universities and were often difficult to distinguish in their policies and practices from the proprietary schools.

This is the grim picture of medical education in the United States in the latter part of the nineteenth century. The European medical centers had so much more to offer that graduates of American schools flocked abroad for further education. In particular, there flourished in the German universities a spirit of

free inquiry coupled with high standards of scholarship that were intensely stimulating and productive.

It was inevitable that attempts should be made to reproduce in American universities the conditions for medical education that had proved so successful in Europe. What was it that the German medical schools had that the American institutions had not? In essence, the difference appeared to lie in the fact that in the German universities the same high standards of scholarship prevailed in the medical schools as in the other graduate departments. This was made possible by the establishment of full-time chairs in the various departments and by the provision of adequate funds and facilities for research. In the medical sciences this meant that a professor was relieved of the necessity of earning his living by carrying on a practice and could devote all his time and energy to the pursuit of knowledge in his chosen field.

In the United States, even in the university medical schools, the teaching was almost entirely in the hands of practitioners, who had little or no contact with the rest of the university. The first reform recommended by the American Medical Association was to lengthen the school year from four months to six months. This radical innovation was successfully opposed by the faculty of Harvard Medical School.[3]

It was the Chicago Medical College (now Northwestern University) that was the first to break away from the traditional system of repeating the same lectures year after year by inaugurating, in 1859, a graded curriculum of three years, of six months each, with an examination at the end of each year.[4]

In 1870 the young president of Harvard University, Charles William Eliot, was able to carry similar reforms through at Harvard Medical School in the face of loud protests from the faculty. Among these reforms was one that put the professors on a salaried basis. Hitherto, their earnings had come entirely from student fees. The salaries were modest, however, and since almost all the instruction was in the form of lectures, the costs of medical education were low and adequately covered by tuition.

The organization of Johns Hopkins University School of Medicine in 1893, under the leadership of William H. Welch, showed clearly the influence of the German universities and included full-time chiefs in all departments. This pattern came to be followed, to some degree at least, by the leading American medical schools. The better schools forged ahead, but the poorer ones stood still. In general, it was the proprietary schools that failed to raise their standards.

While the university medical schools were undertaking radical improvements in their teaching programs the American Medical Association through its Committee on Medical Education had been waging an ineffective battle to raise the standards throughout the country. The forward march of the university schools had accentuated the deplorable condition of the proprietary schools. However, the latter were many and not without influence. There were no less than 7 of them in Louisville, Kentucky, alone. There were altogether *160 medical schools* in the United States, about as many as in all the rest of the world. A number of them were out-and-out diploma mills.

It was obvious that in the interest of the health of the people and of the good name of the medical profession the inferior proprietary schools should be closed down. In an attempt to deal more effectively with this problem the American Medical Association, in 1904, established the Council on Medical Education under the able chairmanship of Arthur Dean Bevan.[2]

Through the medium of the Council standards for medical schools were set up, visits of inspection to the schools were made, confidential reports were made to each school, and the schools were classified as "A", "B" and "C". These activities stimulated a general tightening up of requirements in the medical schools but also aroused resentment in some quarters.

At that point it appeared highly desirable to have a realistic appraisal of the condition of medical education in this country by an impartial group outside the medical profession. With this in mind the Council approached the Carnegie Foundation, which readily agreed to undertake the task. Two years were spent by Dr. Abraham Flexner, of the Foundation, assisted by Dr. N. P. Colwell, of the Council, in inspecting the medical schools. The results of this survey were published in the now famous *Flexner Report* of 1910. The Report was severely critical and strongly recommended a number of measures to improve standards that had previously been urged by the Council.[2]

Wide publicity was given to this report, and results were soon apparent. One by one the weaker schools closed their doors. The total number of schools dropped from 160 in 1905 to 95 in 1915, 85 in 1920 and 80 by 1927. It was a resounding triumph for organized medicine, which had been seeking for so long to rid itself of unsavory bedfellows.

Another influence that began to make itself felt during this period was the Association of American Medical Colleges. This organization was composed essentially of all the approved medical schools as institutional members represented by their deans. They, too, conducted inspections and insisted on maintenance of certain standards for retention of membership. They have also published a journal devoted to medical education—the only one of its kind in the world.

The activities and objectives of the Association of American Medical Colleges and the Council had much in common but did not completely overlap. Roughly speaking, it may be said that the interests of the Association lay more with academic matters of curriculum and technics of education whereas the Council interested itself primarily in the establishment and maintenance of over-all standards. The two groups co-operated informally for many years, and in

1942 a device for more effective collaboration was set up in the form of a liaison committee with representation from each group. This committee meets two or three times a year to discuss problems of mutual interest and makes recommendations back to each of the parent organizations. Both groups are represented in all the inspections of medical schools, and joint reports are made. All in all, it has been a very successful working relation.

So much for the external forces that have shaped the pattern of medical education. Attention is now given to a more intimate view of trends in the medical curriculum.

Medical Curriculum

The flowering of the medical sciences of pathology, bacteriology, chemistry and physiology in the last half of the nineteenth century had so captivated the minds of men as to lead to assumptions that therein all the basic problems of medicine would find their answers. One of the first to raise his voice against this assumption was Dr. James Jackson Putnam, who delivered a Shattuck lecture before the Society in 1899, which was entitled, "Not the Disease Only, But Also the Man." Dr. Putnam[5] expressed himself as follows:

> The great leaders of the scientific centuries to which we belong have indeed turned a cold shoulder on the time-honored methods of cure by faith and fear which had worked miracles for ages past. Their work lay in establishing the reign of exact methods of inquiry, and they would tolerate no systems that rested on a less firm basis. But the movement which the labors of these men of science inaugurated is now secure beyond all hazard, and the time has come to recognize that there are others that may justly lay claim to our attention. We may accept the limitations which the scientific method imposes, even to the point of sacrificing intuition for the sake of a more conscious insight. But we should not admit any arbitrary limitation of the field of inquiry, nor rest content until scientific research has taken all the divinations of instinct into account. The splendid wave of pathological and bacteriological research that has raised the art and science of medicine to its present position of authority has set physicians trying to solve their problems in terms of pathology alone; but it is a matter for congratulation that this wave is being reinforced by another which is sweeping us toward a better knowledge of the secrets of the mental life in health and disease. Perhaps we may even learn thereby to interpret the teaching of pathology itself in a wider sense.

The point of view so aptly phrased by Dr. Putnam half a century ago has begun to receive recognition in the curriculums of medical schools only in recent years. It is significant that he was a psychiatrist, for it was the development of a body of knowledge in this field that clearly indicated the inadequacy of a wholly organic concept of disease. The psychiatrists must be given credit for making the medical profession aware of the inseparability of mind and body and the futility of considering one without the other. They have taught what many a shrewd practitioner sensed—that one cannot fully understand a patient's reaction to his disease without the context of the environmental and emotional influences that impinge upon him. In bringing this point of view to bear on everyday problems of doctor-patient relations psychiatry has made its greatest contribution to medical education. It is giving new perspective to the practitioner and equipping him better to cope with minor emotional disturbances before they become serious.

Another influence in medical education that has aroused teachers from a preoccupation with organs and diseases to a broader consideration of man and his environment has been the increasing interest in preventive medicine. The old-fashioned courses in sanitation and public health have given way to programs more specifically oriented to the applications of preventive medicine in practice. These applications involve an understanding of the environmental factors that influence growth, behavior and health from fetal life to senescence. They imply some acquaintance with social and economic factors so far as they bear on matters of health. The modern teaching of preventive medicine and psychiatry has therefore contributed to a new orientation of medical education toward a more dynamic concept of man in the matrix of his environmental influences. This I believe to be the most significant trend in medical education today.

The incorporation into the medical curriculum of material from the social sciences has been criticized by some who fear that any time whittled away from the exact sciences, which have been the backbone of the curriculum, will weaken the whole structure.[6] It is clear that care must be taken not to lower the standards of scholarship that the exact scientists have carried so high. At the same time medical educators cannot afford to ignore the contributions that newer fields of learning can make to round out the education of a physician.

Another trend in medical education is a reflection of a broad movement in higher education away from specialization. There is a strong body of opinion that, much as specialization has contributed to the advancement of knowledge, it has had a tendency to fragmentize education, and that broad educational objectives have been lost sight of in highly departmentalized programs. The general education programs in the colleges are an attempt to restore unity to the curriculum by relating the parts to the whole. The same tendencies are beginning to manifest themselves in the medical schools.

The traditional medical curriculum has left each department relatively free to teach its own subject in its own way. It has been assumed that the student could and would integrate what he had learned in each separate course into a well rounded medical education. That is an assumption that is now being questioned. There are those who believe that the student who is immersed in one highly specialized course after another loses sight of the central focus of medical education, which is the sick human being. Departmentalization of teaching has tended to concentrate attention on the parts rather than the whole man and may produce physicians with limited points of view.

Attempts to meet these objections to the traditional curriculum have been along two lines working toward, first, the elimination or bridging of departmental barriers and, secondly, keeping the central objective in focus at all times.

Departmental Barriers

Various technics have been devised for providing better correlation or integration of teaching between departments by special joint exercises, joint courses or joint examinations. At Colorado, for instance, there is considerable collaborative teaching beginning with the first year in which both the basic-science and clinical faculty participate.[6] Clinical applications of the basic sciences are demonstrated on patients to the beginning medical students, whereas later on, in the clinical years, the student sees the biochemist, the pharmacologist and the anatomist participating in the discussion of problems in the clinic. It is hard to appreciate how difficult such apparently simple maneuvers can be. The polished clinician may find himself at a loss to express himself in terms understandable to freshman medical students, and the basic scientist may feel like a fish out of water on the wards. However, in a friendly and co-operative atmosphere these difficulties are not insurmountable. It is recognized that there are dangers in slanting the basic sciences heavily toward clinical applications. If this is pushed too far it can rob basic science of its true significance as the fertile mother of them all and make of her a mere nursemaid, and a sterile one at that. Here, as in so many phases of education, a proper balance must be struck.

Cornell affords another illustration of integrated medical teaching. For six months of the senior year the departments of medicine, preventive medicine, pediatrics and psychiatry join forces in a program of teaching comprehensive medical care during which the student can observe individual patients over a more extended period than is ordinarily possible. This program is designed to transmit to students a concept of "patient-oriented medical care rather than physician-oriented segmental care."[7]

The new curriculum at Western Reserve is the most radical departure from tradition in that the basic sciences are taught not as separate courses but as a single integrated course in human biology. All these innovations in medical education are in the direction of a less specialized and less segmented approach.

Central Objective

And now one should mention attempts to keep the central objective in focus throughout the medical curriculum. The assumption is that the central objective of medical education is an understanding of man in his environment—in other words, of human biology. If that is the objective one should present it to the student early in his course and not let him lose sight of it. There are many who believe that the traditional curriculum fails to do this and that students who have entered medical school with highest motivation become hardened by the impersonal presentation of the basic sciences. Attempts have therefore been made to bring first-year students into personal contact with patients. These have varied in form from clinics for freshmen, which Harvey Cushing conducted so successfully thirty years ago, to the program at Western Reserve, which assigns each freshman student to an expectant mother whose child he will follow throughout his four years. It is difficult to appraise the value of devices such as these, which are designed to influence attitudes rather than to impart factual knowledge. One can say that in general the response of the students is gratifying, and one cannot help observing that these seeming innovations actually are harking back to the patient-oriented teaching of a century and a half ago—to the days before the student was taken away from the bedside to the lecture room and the laboratory.

Costs of Medical Education

No discussion of medical education would be complete without some mention of the financial situation that the schools are now facing. To state the problem in a nutshell, costs have increased much more than income from endowment and tuition. Income and inheritance taxes have diminished accruals to endowment, and tuition fees currently bring in only about 20 per cent of the cost of instruction. The net result is that the schools as a group are being operated at a substantial loss. To the tax-supported schools this does not offer a serious threat, but it means that some of the privately supported schools must find new sources of income or close up shop. The nation's physicians, through their alumni associations and through the American Medical Education Fund, and the nation's industry and business, through the National Fund for Medical Education, are making a valiant attempt to meet this critical need. These groups probably represent the last remaining potential source of large-scale private support. To date the funds that they have raised have been helpful but insufficient. There is still some hope that the National Fund can rally more substantial support from industry, but at the moment it seems unrealistic to assume that private funds will be adequate to continue the full support of the private schools. It is beginning to look as if there would have to be more support from tax sources to the private schools if they are to survive.

One interesting development in this regard has been the organization of regional compacts between states for the support of higher education, including medical, dental and veterinary education. The Southern Regional Education Board has been in successful operation for five years, and a similar plan has recently been organized in the Rocky Mountain States. These regional compacts serve as agencies through

which a state that has no medical school may contract with a medical school outside the state but within the region to give a certain number of its qualified residents a medical education and to pay the institution the full cost. Such a plan is being proposed for the New England area and has much to commend it. It offers each participating state a more economical way of obtaining medical education for its residents than by establishing a separate school of its own. At the same time it should exert a stabilizing influence on the medical schools of the region by sharing the costs of operation.

Summary

I have traced the evolution of medical education in this country from its rude beginnings as a simple apprenticeship to its present status as a highly organized field of learning. I have indicated the role that the profession itself has played in this development, with some illustrations from the history of the Massachusetts Medical Society. I have reported on some recent trends in the direction of a more unified curriculum in the medical schools. And, finally, I have pointed out that in the process of improvement in medical education the costs have risen so high as to raise serious problems for the schools that are not tax supported.

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INCREASED INTRACRANIAL PRESSURE CAUSED BY INCREASED PROTEIN CONTENT IN THE CEREBROSPINAL FLUID*

An Explanation of Papilledema in Certain Cases of Small Intracranial and Intraspinal Tumors, and in the Guillain–Barre Syndrome

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THE thesis of this paper is that increased intracranial pressure and communicating hydrocephalus may result from any chronic process that significantly raises the level of the protein content of the cerebrospinal fluid. The increase in pressure is due to mechanical clogging, by the protein molecules, of the pores of the semipermeable membrane that constitutes the brain-blood barrier. That cellular and fibrinous exudate can obstruct these absorptive areas is well recognized. The possibility that objects the size of protein molecules can have the same effect has not previously been investigated. Interest in this subject was aroused by a case of ependymoma of the cauda equina in which the presenting symptom was failure of vision due to papilledema, by a second case in which a small acoustic-nerve tumor produced an advanced degree of communicating hydrocephalus and by a third in which papilledema accompanied the Guillain–Barré syndrome.

Butt and Keys[1] found in vitro that protein molecules will diminish the porosity of semipermeable membranes. They showed, for instance, that there are ranges of collodion membranes that are permeable to gum acacia in the absence of blood serum but perfectly impermeable to acacia in the presence of serum.

Chambers and Zweifach[2] demonstrated a similar phenomenon in vivo. In the frog's mesentery they found that an important component of the living capillary wall is a thin noncellular layer of condensed protein lining the inner surface of the endothelium. They noticed that during perfusion with crystalloid solutions, this thin noncellular layer sloughed off, after which the perfused fluid passed rapidly through the leaky capillary wall, with resulting edema of the tissues. Changing the perfusate to one containing serum resulted in the reappearance of the thin, noncellular layer and an appreciable reduction in the edema. The authors concluded that this adsorbed layer of protein molecules on the endothelial lining of the capillaries diminishes its porosity.

Ependymoma of the Cauda Equina Producing Papilledema

Case 1. A 52-year-old woman was admitted to the hospital in February, 1945, because of failing vision of 2 months' duration. Five years previously she had experienced her 1st episode of loss of vision. She consulted a physician, who found the optic disks to be elevated 1 or 2

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diopters, and the veins engorged and tortuous. A spinal puncture disclosed "increased globulin content." She was given fever treatment and thiamine chloride, and the visual symptoms improved. The present episode of failure of vision was unaccompanied by headache or vomiting.

Physical examination showed bilateral papilledema of 2 diopters, with secondary optic atrophy, more pronounced in the right eye. In this eye the patient was barely able to count fingers at a distance of 30 cm. There was a central scotoma. In the left eye the visual acuity was 6/9, and there was a paracentral scotoma in the lower portion of the field. There were no other findings of significance except absence of the Achilles-tendon reflexes.

The spinal-fluid pressure was equivalent to 325 mm. of water. The pressure rose to 520 on jugular compression for 10 seconds and then returned slowly to the initial level. The fluid was yellow. It contained no cells. The total protein was 425 mg. per 100 cc. After the spinal puncture pain developed in the right sciatic area. Twelve days later the spinal-fluid pressure was equivalent to 350 mm. of water. The total protein on this examination was 227 mg. per 100 cc. On the following day a cisternal puncture was performed, and the total protein of the cisternal fluid was 50 mg. per 100 cc. Lipiodol, 0.5 cc., was injected into the cisterna, and with the patient in the erect position an x-ray examination was made, showing the Lipiodol to be arrested at the level of the 3d lumbar vertebra. Despite the unexplained papilledema it was decided to investigate the cause of the spinal subarachnoid block.

A lumbar laminectomy was performed by removal of the laminae of the 2d, 3d, and 4th lumbar vertebras. The dura was opened, and a large, vascular, encapsulated tumor filling the entire area of the exposure was removed. The microscopical diagnosis was ependymoma.

The patient made a satisfactory convalescence, and at the 2-month follow-up examination, the disks were flat and atrophic. The visual acuity and the visual fields were the same as before the operation. The patient was last seen 5 years later, when there had been no further attacks of visual loss and no pain in the legs. She was working regularly as a domestic servant.

In this case it is unfortunate that a specimen of cisternal fluid was not obtained at the time of the first spinal puncture. On the day after the second spinal puncture a sample of cisternal fluid was removed and found to contain only 50 mg. of protein per 100 cc. The protein content of the lumbar fluid dropped from 425 to 227 mg. per 100 cc. in the interval between the two lumbar punctures. We believe that the protein content of the cisternal fluid was probably higher than this before spinal puncture but that it subsequently became reduced as a result of dilution with ventricular fluid occasioned by a continuing leak of cerebrospinal fluid at the site of the lumbar punctures.

Fincher[3] reported 5 cases of tumors of the cauda equina in which the symptoms consisted of attacks of spontaneous subarachnoid hemorrhage. Except for some associated lumbar or leg pain the episodes resembled typical attacks of spontaneous subarachnoid hemorrhage due to ruptured berry aneurysm. In 3 of Fincher's cases the histologic diagnosis was ependymoma. The spinal fluid was bloody, the pressure was elevated, and a spinal subarachnoid block was not present.

The case described above cannot be considered one of Fincher's syndrome because the symptoms did not suggest subarachnoid hemorrhage, and the fluid contained no blood. Instead of headache the presenting symptom was loss of vision. We believe that the increased intracranial pressure was due to delayed absorption of cerebrospinal fluid resulting from clogging of the pores of the brain-blood barrier by a layer of protein molecules.* We believe that the increased protein in the cerebrospinal fluid arrived there as a transudate through the imperfect walls of the blood vessels of the ependymoma. Further evidence of imperfection in the blood-vessel walls of these tumors is demonstrated by their tendency to bleed, thus producing the syndrome described by Fincher.†

Love, Wagener and Woltman[4] reported 3 cases of papilledema due to tumor in the spinal canal. Their first patient was a twelve-year-old boy with papilledema and communicating hydrocephalus produced by an ependymoma of the cauda equina. The ventricular fluid was grossly yellow and somewhat opalescent. Air introduced into the ventricles disclosed Grade 3 hydrocephalus, with some of the injected air escaping into the basal cisterna. The total protein of the ventricular fluid was 180 mg. per 100 cc., with 1 lymphocyte per cubic millimeter and many erythrocytes. Spinal fluid obtained from the lumbar canal coagulated. The ependymoma was removed, and the papilledema was subsiding when the patient was discharged from the hospital on the sixteenth postoperative day. Eight months later the optic disks were flat, and the vision normal.

Their second patient was a man of forty-four who had a recurrent oligodendroglioma in the lower thoracic portion of the spinal cord. He had papilledema of 4 to 5 diopters. The cisternal fluid, which was grossly yellow and hemorrhagic, contained 160 mg. of protein per 100 cc. and 28,000 red blood cells per cubic millimeter, with 54 lymphocytes and 8 polymorphonuclear leukocytes. A cisternal encephalogram was performed and showed a mild hydrocephalus. The papilledema was subsiding at the time of his discharge sixteen days after laminectomy and removal of the tumor.

Their third patient was operated on by Adson in 1925. This woman had papilledema of 4 diopters, a complete block and yellow spinal fluid. The cisternal puncture disclosed pale-yellow fluid. The ventricular fluid was "clear." A cerebellar exploration disclosed no tumor. An ependymoma was removed from the lumbar canal, and the papilledema subsided. Five years later the patient was well.

These authors concluded that the papilledema in these cases was secondary to a complete block of the circulation of the spinal fluid at the site of the tumor in the spinal canal. However, they also stated that "papilledema without primary loss of vision seems to be due occasionally to an increase in the protein content of the cerebrospinal fluid."

*The osmotic tension of the protein molecules contributed only in small part to the increased pressure of the cerebrospinal fluid. A solution containing 300 mg. of blood proteins per 100 cc. of water exerts an osmotic tension of only 0.7 mm. of mercury.

†The inadequacy of the walls of neoplastic blood vessels in general is illustrated in cases of hemangiomatous cysts of the cerebellum. In these cysts the obvious source of the protein-rich fluid is the escape of blood plasma through the walls of the blood vessels that constitute the neoplasm.

Kahn and Luros[5] described a case of advanced communicating hydrocephalus produced by a papilloma of the glomus of the choroid plexus of the lateral ventricle. This tumor did not in any way obstruct the circulation of the cerebrospinal fluid, and the authors assumed that the hydrocephalus was caused by an overproduction of cerebrospinal fluid, with the tumor functioning "as a tremendously hypertrophied choroid plexus." They did not mention the protein content of the ventricular fluid, but in a personal communication Dr. Kahn stated that it was 54 mg. per 100 cc. We agree with the authors that this tumor was producing fluid, but we suspect that the increased protein content of the fluid, rather than the actual volume of the fluid produced, caused the hydrocephalus.

Small Acoustic Tumor Producing Communicating Hydrocephalus

Case 2. A 44-year-old woman complained of fainting spells and headaches, which had been present for 2 years when she was first seen in October, 1951. She had been studied 15 months previously, when spinal puncture disclosed a pressure fluctuating between 180 and 400 mm. of water. The total protein was 400 mg. per 100 cc. A pneumoencephalogram at that time was performed, 250 cc. of cerebrospinal fluid being replaced by a similar quantity of air. The films disclosed a communicating hydrocephalus of such advanced degree that the volume of air injected was only sufficient to fill one lateral ventricle at a time.

The patient was observed in one of her attacks of headache. She was found to have profound nystagmus on right gaze. A few minutes later this had disappeared. There was no papilledema. In response to direct questioning she stated that she thought her hearing was slightly impaired, but there was no difference on the two sides. There were no other neurologic signs. The possibility of an intraspinal tumor (as in Case 1) was considered, and a combined lumbar and cisternal puncture was carried out. As at the previous puncture the pressure was found to fluctuate widely, but it finally stabilized temporarily at 150 mm. of water. On jugular compression the pressure rose promptly, the rise being simultaneous in both manometers. The pressure returned to the previous level in 20 seconds. The lumbar fluid contained 1 cell per cubic millimeter and the Pandy reaction was ++++. The total protein was 180 mg. per 100 cc. in the cisternal and 200 mg. per 100 cc. in the lumbar fluid. The possibility of a cerebellar tumor was then considered because of the appearance of nystagmus on one examination, because of the increased protein content of the cerebrospinal fluid and despite the fact that encephalography carried out 18 months previously had shown the hydrocephalus to be of the communicating variety.

On November 1 a midline suboccipital craniotomy was performed. The dura was incised, disclosing a large cisterna magna with no herniation of the cerebellar tonsils. The lower end of the 4th ventricle was wide open. There was no lateral dislocation of the pons. The diagnosis was obviously communicating hydrocephalus. A retractor was introduced along the right side of the pons, and no abnormality was encountered. On the left side, as the lateral surface of the pons was exposed, a 2-cm., globular, encapsulated tumor came into view. An incision was made in the capsule of the growth, and the contents removed with a curette. By gentle traction the tumor capsule was gradually mobilized and freed from its delicate attachment to the brain stem. The 7th nerve was found to be attached to the anterior surface of the growth. It separated readily, by blunt dissection. Finally, the entire tumor was removed, including a small nubbin that lay in the porus acousticus and indicated its 8th-nerve origin. The 7th nerve was identified by electric stimulation and found to be intact from the pons to the porus. What appeared to be the 8th nerve lay below the 7th nerve, and it also appeared to be largely intact. The histologic diagnosis was neurilemoma.

The patient had a long and stormy postoperative convalescence. She had complete paralysis of the left 7th and 8th cranial nerves. She experienced such severe vertigo and nausea that, 7 weeks after operation, a feeding jejunostomy was necessary to improve her nutrition. These symptoms were assumed to be due to irritation of the traumatized 8th nerve. One year after operation she was free of symptoms except for deafness in the left ear and paralysis of the left facial nerve that was clearing. The spinal-fluid pressure was equivalent to 40 mm. of water, and the protein 31 mg. per 100 cc.

Guillain–Barre Syndrome with Papilledema

Case 3.* This patient was a 26-year-old woman with slowly progressive paralysis of the lower extremities and facial paralysis. The symptoms began in the 4th month of pregnancy and reached their maximum shortly after delivery. During the 7th month of the illness she complained of headache and was found to have bilateral papilledema. The spinal-fluid pressure was equivalent to 600 mm. of water. The total protein was 470 mg. per 100 cc. The papilledema subsided after a subtemporal decompression.

Drew and Magee[8] collected 10 cases of papilledema in the Guillain–Barré syndrome. Table 1 presents a summary of the findings in the cases that they report. The authors concluded that the papilledema that

Table 1. *Papilledema in the Guillain–Barré Syndrome.**

Case No.	Cerebrospinal-Fluid Protein	Cerebrospinal-Fluid Pressure	Papilledema
	mg./100 cc.	*mm. H_2O*	
1	420	600	3 diopters
2	200	400	2 to 3 diopters
3	400	330	2 to 3 diopters
4	("Increased")	(Not mentioned)	3 diopters
5	2080	+150	Present
6	268	("Normal")	"Definite papilledema"
7	over 1000	130	"Transitory papilledema"
8	286	(Not mentioned)	"Slight"
9	815	350	Present
10	490	250	3 diopters (right eye); slight (left eye).

*Based on cases collected from literature by Drew & Magee,[8] including their own case (Case 10).

occurs in the late stages of this syndrome cannot at present be adequately explained. Denny-Brown[9] also described a case of papilledema associated with the Guillain–Barré syndrome. He attributed the increased intracranial pressure to clotting in vivo of the cerebrospinal fluid, with obstruction of the pacchionian bodies.

Papilledema in Poliomyelitis

Weiman, McDowell and Plum[10] observed papilledema in 5 severely paralyzed patients in the convalescent stage of acute poliomyelitis. It appeared eleven to forty-eight days after the onset of the illness and lasted thirteen to one hundred and forty days. It was a benign and self-limited complication. Each patient complained of double vision, and 1 had associated headache. The visual acuity and visual fields were normal in each of the 5 patients. These authors concluded that the papilledema was part of a generalized

*Previously reported by Dempsey et al.[6] and Ford and Walsh.[7]

edema of the central nervous system associated with infection. Their findings are summarized in Table 2.

A survey of this material indicates that in the production of papilledema, the chronicity of the process is more significant than the level of the protein concentration. This, in turn, suggests that the increased pressure is due to the piling up of the protein molecules against the brain-blood barrier rather than to the increased osmotic tension of the protein-rich fluid.

TABLE 2. *Papilledema in Poliomyelitis.**

CASE NO.	CEREBROSPINAL-FLUID PROTEIN	CEREBROSPINAL-FLUID PRESSURE	PAPILLEDEMA	DURATION OF OBSERVED PAPILLEDEMA
	mg./100 cc.	*mm. H_2O*		
1	(No lumbar puncture)	—	2 diopters	10 wk.
2	147	180	2 diopters	30 days
3	162	390	3 diopters†	12 days
4	99	140	3 diopters‡	2½ wk.
5	306	600	4 diopters	20 wk.

*Based on cases of Weiman et al.[19]
†12 days after lumbar puncture optic fundi had returned to normal.
‡Papilledema developed 1 wk. after this lumbar puncture.

In the cases of poliomyelitis the papilledema was discovered earlier, within eleven to forty-eight days of the onset. In this condition, however, there was cellular exudate in addition to protein-rich fluid to clog the barrier. As illustrated by our Case 2 a single observation of normal spinal-fluid pressure in these cases should not mislead the observer into ascribing the disk edema to some mechanism other than increased intracranial pressure, because the pressure may fluctuate widely from minute to minute in the individual case.

INVESTIGATIVE PROCEDURES

Experiment 1

In the dog we attempted to produce papilledema by repeated cisternal injections of human albumin and gamma globulin. These attempts failed. We found that the injected protein disappeared from the fluid more rapidly than had been anticipated. If albumin was injected in amounts sufficient to increase the protein content of the cerebrospinal fluid to 1000 mg. per 100 cc. the protein content of cisternal fluid was down to 100 to 200 mg. per 100 cc. five hours later and was virtually back to normal within twenty-four hours. This rate of disappearance suggests that to cause a significant rise in total protein content, the escape of protein into the fluid must be fairly rapid.

Experiment 2

In an effort to demonstrate whether a protein-rich fluid is absorbed more slowly from the subarachnoid space, the following experiment was carried out: a test dog and a control dog weighing 8.8 and 9.4 kg. were anesthetized with Nembutal and placed on their left sides, and a cisternal puncture was performed with a 20-gauge needle. This needle was in turn connected to rubber tubing, one arm of which went to a manometer and the other arm to a calibrated reservoir containing Ringer's solution. The initial cisternal pressure in each animal was equivalent to 150 mm. of water. The reservoir of Ringer's solution was elevated to a height of 300 mm. above the cisternal needle, and was held constantly at this level by the gradual addition of Ringer's solution as the fluid was absorbed from the subarachnoid space. In the test dog it was necessary to add 11.4 cc. of Ringer's solution to maintain the pressure at 300 mm. of water for the first hour. In the control dog it was necessary to add 10.2 cc. of Ringer's solution over this same period to maintain the pressure of 300 mm. of fluid.

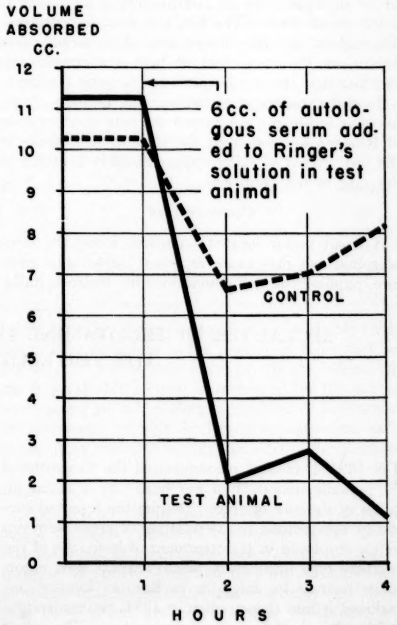

FIGURE 1. *Rate of Absorption of Ringer's Solution Introduced into the Cisterna Magna at a Constant Pressure Equivalent to 300 mm. of Water.*

The solid line indicates the rate before and after the addition of autologous serum in the test animal, and the broken line the rate in the control animal.

These figures were taken to represent the rate of absorption of fluid from the cerebrospinal axis in the respective dogs at this head of pressure. Six centimeters of autologous serum was then injected into the rubber tubing close to the cisternal needle in the test dog, and a similar quantity of Ringer's solution

was withdrawn from the reservoir so that the level of the fluid remained 300 mm. above the cisternal needle. During the first hour after the introduction of the serum 2.0 cc. of fluid was absorbed by the cerebrospinal axis in the test animal. In the control animal 6.8 cc. of fluid was absorbed. In the second hour 2.6 cc. was absorbed in the test dog and 7.0 cc. in the control. In the third hour 1.1 cc. was absorbed in the test dog and 8.1 cc. in the control (Fig. 1). The tubes leading to the respective reservoirs were then clamped, the spinal-fluid-pressure manometer being left attached to the cisternal needle. Ten minutes later the pressure in the manometer in the test animal, which had gone up to 310 mm. at the time of clamping, remained at that level. By this time the pressure in the manometer in the control animal had fallen to 230 mm. of water. The test was then discontinued. Throughout the experiment arterial pulsations were present in the meniscuses of both manometers, indicating that the needles had not become displaced.

In this experiment, therefore, the addition of autologous serum protein caused the rate of absorption of Ringer's solution from the subarachnoid space in the test animal to fall to approximately a fourth of the rate in the control.

Conclusions

A small tumor located anywhere along the cerebrospinal axis may cause increased intracranial pressure, papilledema and communicating hydrocephalus. This is due to the escape of serum protein into the cerebrospinal fluid through the imperfect walls of the blood vessels of the neoplasm. The protein molecules become piled up against the semipermeable membrane that constitutes the brain-blood barrier. This progressive deposition causes partial obstruction of the absorptive areas of the cerebrospinal fluid, with resulting rise in pressure. The same process may operate in the Guillain–Barré syndrome to produce papilledema. This process is completely reversible as contrasted to that which occasionally follows a purulent meningitis.

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RECTAL USE OF ERGOTAMINE TARTRATE AND CAFFEINE ALKALOID FOR THE RELIEF OF MIGRAINE*

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IN 1894 Thomson[1] recommended the treatment of "periodic neuralgia of the head" by a rectal infusion of tincture of ergot. Despite the reported success of this method the derivatives of ergot were not widely employed in the treatment of headache of the migraine type until 1928, when Tzanck[2] used ergotamine tartrate for migraine in Europe; Lennox[3] introduced it into this country in 1934, recommending both oral and parenteral administration. The rectal route seems to have been neglected until the past three years, when several observers[4,5] reported the efficacy of ergotamine tartrate and caffeine alkaloid for migraine when used in the form of a rectal suppository.

Method of Study

Since many sufferers from migraine cannot arrange to get ergotamine tartrate hypodermically at the onset of an attack and many are too nauseated to tolerate ergotamine tartrate by mouth or else find it ineffective by that route, it seems worth while to call attention again to the fact that the rectal route for this medication often affords a successful solution to this dilemma. Patients who initially use rectal suppositories of ergotamine tartrate and caffeine, prompted by the reasons given above, often find that the method is so efficacious and so unproductive of unpleasant side effects that they make it routine thereafter. The present report concerns the efficacy of various combinations of ergotamine tartrate and caffeine alkaloid and in some cases atropine derivatives as used rectally by 100 patients in 577 attacks of migraine. During the period of this study many additional patients were treated by this method during numerous attacks of headache, and in general the results in this untabulated group corroborated the more accurate data kept on the smaller or "study group."

The patients in the "study group" were urged to use the suppository as soon as they were sure a gen-

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uine migraine attack was under way. This was emphasized since it is well known that ergotamine tartrate is most effective when taken early in the attack.

Results

Various plans of treatment were tried in an attempt to find the most useful unit and method of dosage. The amount of medication required by different patients and by the same patient in different attacks varied considerably. Results were classified as "good" if the headache was completely relieved within three hours, "fair" if the headache was completely relieved between three and six hours after the suppository was taken and "poor" if the headache was not relieved within six hours (Table 1). Unpleasant side effects were scored as "mild," (consisting only of nausea), "moderately severe," (consisting largely of nausea and vomiting), and "severe," (making the use of the medication in that dosage of questionable value). "Severe" reactions consisted of nausea, vomiting, muscle cramps, lassitude and prostration. Most of the side effects were attributed to the ergotamine tartrate. There were a few patients who suffered nervousness, tremor and insomnia. These symptoms were thought to be due to the caffeine. An effort to offset nausea and vomiting by the addition of atropine to the suppository did not prove particularly effective and made one more element to deal with in the matter of adjusting dosages. Local rectal irritation was not encountered even in patients who used the suppositories very often (three times a week). In a few cases in which a water-soluble glycerin base was used the suppository produced a bowel movement and usually prevented the systemic absorption of its contents. For this reason the suppositories containing a cocoa-butter base were preferred, although precautions had to be taken to prevent them from melting by keeping them in a refrigerator.

In the evaluation of the combination of drugs most effective in stopping a headache and least productive of unpleasant side effects the general impression was gained that the dose of 1 mg. of ergotamine tartrate and 100 mg. of caffeine alkaloid provided the most useful unit. For some patients, this was not enough, and either the dose had to be repeated in an hour or, on another occasion, twice the original amount was used in the first place. On the other hand the suppository had to be cut in half for patients who were very sensitive to the action of these drugs. A certain amount of experimentation by both patient and doctor was necessary to determine the smallest quantity of ergotamine tartrate that would produce relief for a given person in a satisfactory manner. For patients who proved sensitive to the caffeine alkaloid in the suppository, it was necessary to omit this from future prescriptions. The tailoring of prescriptions to individual needs proved to be an important element in the successful management of the problem.

A glance at the totals in Table 1 reveals that ergotamine tartrate and caffeine alkaloid in variable doses used by the rectal route for 577 attacks of migraine produced good results in 423, or 73 per cent, fair results in 101, or 17 per cent, and poor results in 53, or 10 per cent. There were only 30 cases (5 per cent) in which unpleasant side effects were reported. With 2 exceptions these were only "mild" or "moderately severe."

These results suggest that the rectal route of administration of ergotamine tartrate and caffeine alkaloid for migraine is highly effective, probably ranking next in reliability to the parenteral route and being superior to the oral route in efficacy. Certainly, this is a valuable method of treatment for the patient who cannot get a hypodermic injection of ergotamine tartrate easily or who is already so nauseated early in his attack that oral medication is out of the question.

Table 1. *Results of Rectal Use of Ergotamine Tartrate.*

Drug	No. of Patients	No. of Trials	Good Result	Fair Result	Poor Result	Unpleasant Side Effects		
						Mild	Moderate	Severe
			%	%	%	%	%	%
Rectal suppositories of ergotamine tartrate and caffeine alkaloid	100	577	73	17	10	4.3	0.16	0.03
Cafergot tablets (used rectally)	18	180	38	47	15	0	1.0	0

Discussion

More recently, some patients have been told to insert a Cafergot* tablet in the rectum (these tablets contain 1 mg. of ergotamine tartrate and 100 mg. of caffeine alkaloid). Although they are ordinarily designed for oral medication, increasing experience shows that these tablets are well tolerated by rectum and are probably more effective by that route in smaller dosage than they are by mouth. In some cases the dose had to be repeated after an hour. Several patients found that they had to take up to 6 tablets of Cafergot by mouth to relieve an attack, whereas 1 or 2 tablets by rectum brought about the desired effect even more promptly. In a small study group in which Cafergot tablets were used by rectum, 180 attacks in 18 people were treated by this method. The results were good in 69, or 38 per cent, fair in 85, or 47 per cent, and poor in 26, or 15 per cent.

*Kindly supplied by Sandoz Chemical Works, Incorporated, New York City.

There were "moderately severe" side reactions in 2 (1 per cent). Although the ergotamine tartrate and caffeine alkaloid embodied in a cocoa-butter suppository seem to offer the more efficacious method of applying these medicines as rectal therapy, the Cafergot tablet as used in the rectum has the advantages of being easily carried in the handbag, and thus used early in the attack if necessary, and of economy so far as the price is concerned.

I am indebted to Miss Virginia Bloom for her patient help in collecting these data.

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ULTRAFILTRATION STUDIES ON SERUM MAGNESIUM*

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OF the four major cations in human extracellular fluid, magnesium has been investigated least. This neglect may be attributed in part to difficulties in methodology, since serum contains only 1 or 2 milliequiv. of magnesium per liter. The magnesium ion, however, is a large component of intracellular fluid and bone. Numerous animal studies have demonstrated its dietary importance in intermediary metabolism.[1-4] Low concentrations of serum magnesium have been reported in patients with rickets caused by vitamin D deficiency,[5] diabetic ketosis during insulin therapy,[6] and dietary phosphate load[7,8] and in a child with chronic tremor and a bony lesion thought to be Legg–Perthes disease.[9] Hirschfelder[10] described low concentrations of serum magnesium in chronic nephritis, hypoparathyroidism, a patient with idiopathic epilepsy and a patient with eclampsia.

Abnormally elevated serum magnesium concentrations have occurred in diabetic coma before insulin therapy[6] and in acute and chronic glomerulonephritis.[10] Two groups of workers investigated total and ultrafiltrable magnesium in the serum of adults with hypothyroidism and hyperthyroidism and found an increase in the ultrafiltrable fraction in hypothyroidism and a decrease in hyperthyroidism, with no change in the total serum magnesium concentration.[11-13] Later investigators were unable to confirm these findings.[14,15]

The present study was initiated to define the values for total and ultrafiltrable magnesium in the serum of normal children and children with several of the entities alluded to above. A few adults were also studied.

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Methods

The control series in this study was composed of children taken to the Out-Patient Department of the Harriet Lane Home with minor complaints and children hospitalized for surgical procedures. The patients with pathologic entities were seen in special clinics or the wards of the Harriet Lane Home and the Johns Hopkins Hospital.

Ultrafiltration of serum was performed as described by Lavietes[16] and modified by Hopkins, Howard and Eisenberg.[17] The serum was first equilibrated with carbon dioxide gas, after which ultrafiltration was done under a pressure equivalent to 20 cm. of mercury. The pH of the ultrafiltrate was found to range between 7.35 and 7.65, a Beckman pH meter being used. Magnesium concentrations of serum and serum ultrafiltrate were measured in duplicate by the titan-yellow micromethod of Orange and Rhein,[18] modified by the use of 0.2 cc. of serum or ultrafiltrate, which necessitated final mixing in 10-cc. volumetric flasks. Polyvinyl alcohol was used as a dispersant for the titan-yellow-magnesium lake. The final color was read at 560 millimicrons in a Coleman universal spectrophotometer, with the use of microcuvettes with a 50-mm. light path as devised by Sobel and Snow.[19] Measurements of total protein concentration were made by the gradient tube method of Linderström–Lang as modified by Lowry and Hunter.[20]

Results

Data on Normal Infants and Children

Table 1 presents information obtained on a group of 43 normal infants and children, three months to twelve years of age. These control values for total serum magnesium, ultrafiltrable magnesium and percentage of ultrafiltrable magnesium are quite similar to data on adults in the literature.[14,15,18,22-24] The mean values for total serum magnesium and percentage of ultrafiltrable magnesium in the controls are

identical with those for such determinations made on adults by Copeland and Sunderman.[24] There appeared to be no change in any of the values with increasing age. The concentration of "ionized" magnesium in the ultrafiltrate was estimated from serum total magnesium and serum total protein by means of the nomogram of Willis and Sunderman.[21] No significant difference was found between measured ultrafiltrable magnesium and "ionized" magnesium calculated from the nomogram in the control series.

Data on Patients

Table 1 also gives data on a group of nephrotic children, demonstrating normal values for protein-bound magnesium even though the serum total protein was grossly diminished. Observations on groups of children with epilepsy, Legg–Perthes disease and infectious hepatitis revealed no significant deviations of the total or ultrafiltrable serum magnesium values from normal. Results on 5 congenital cretins and 2 children with juvenile hypothyroidism did not confirm the previous reports of increased ultrafiltrable magnesium in hypothyroidism.[11-13]

Table 2 presents data obtained on a group of patients with diseases who had been selected for study because of suggestive findings in the literature. Of 3 patients with idiopathic hypoparathyroidism studied, 1 had perfectly normal values, 1 had a questionably depressed serum total magnesium, and the third had a definitely low ultrafiltrable magnesium fraction (Case 2). The highest total serum magnesium values were found in 3 cases of chronic renal insufficiency (Cases 4-6).

Sharp post-morten rises in serum total magnesium concentration were found in Cases 7 and 8.

During the course of this study 2 patients were observed, each of whom showed a striking disparity between serum magnesium and serum calcium concentration. These cases were as follows:

Case 9. This woman with idiopathic steatorrhea had a history of diarrhea for about 2½ years, with several remissions and relapses. On entry to the Johns Hopkins Hospital she was very cachectic, with a serum calcium of 5 mg. and a serum inorganic phosphorus of 2 mg. per 100 cc. She was placed on a high-calcium, high-protein, low-fat diet, with 200,000 units of vitamin D a day. She improved for a few weeks, but when the observations of the serum ultrafiltrable magnesium were made she was again having 5

TABLE 1. *Mean Values for Serum in Normal Children and in Children with Disease.*

Group	Age Range	Total Magnesium	No. of Patients	Ultrafiltrable Magnesium	No. of Patients	"Ionized" Magnesium*	No. of Patients	Total Protein	No. of Patients	Percentage of Ultrafiltrable Magnesium	No. of Patients
		milliequiv./liter		*milliequiv./liter*		*milliequiv./liter*		*gm./ 100 cc.*			
Controls		1.77		1.16		1.23		7.80		65.3	
S. E.†	3 mo.–12 yr.	0.02	43	0.02	36	0.02	29	0.13	32	1.8	35
Patients with Nephrosis		1.58		1.08		1.26		3.85‡		70.0	
S. E.†	3 mo.–6 yr.	0.12	7	0.07	7	0.16	4	0.53	4	5.1	7

*"Ionized" magnesium calculated from monogram of Willis and Sunderman.[21]

†Standard error of mean = $\sqrt{\frac{\Sigma\Delta^2}{N(N-1)}}$

‡Figure differs significantly ($P = 0.02$) from value of corresponding control group.

TABLE 2. *Values for Serum in Patients with Various Diseases.**

Case No.	Diagnosis	Total Magnesium	Ultrafiltrable Magnesium	Percentage of Ultrafiltrable Magnesium
		milliequiv./liter	*milliequiv./liter*	
1	Idiopathic hypoparathyroidism	1.66	1.14	69
2	Idiopathic hypoparathyroidism	1.66	0.29	17
3	Idiopathic hypoparathyroidism	1.27	1.00	79
4†	Chronic nephritis	5.24	4.40	84
5†	Chronic nephritis	5.46	—	—
6†	Chronic nephritis	3.06	—	—
7	Prematurity; chronic hypothermia.	1.81	(6 hr. ante mortem)	
		2.58	(Immediately post mortem)	
8	Rheumatic heart disease	1.70	(30 min. ante mortem)	
		3.80	(Immediately post mortem)	

*Unless otherwise noted, patients are preadolescent children.
†Adult.

or 6 fatty stools a day, with weakness and anorexia. At this time she had a serum total magnesium concentration of only 0.29 milliequiv. per liter and an ultrafiltrable concentration of exactly the same figure; 100 per cent of the serum magnesium was ultrafiltrable. The total serum calcium was 7.7 mg. per 100 cc. (3.8 milliequiv. per liter) and "ionized" serum calcium, calculated by the nomogram of McLean and Hastings,[25] was 4.2 mg. per 100 cc. The serum total protein concentration was 4.6 gm. per 100 cc., of which 3.1 gm. was albumin. The serum inorganic phosphorus was 3.0 mg., and the nonprotein nitrogen 28 mg. per 100 cc. Urinalysis was negative. There was no anemia.

Case 10. M.W., (J.H.H. A55193), a 7-year-old Negress, was admitted to the Harriet Lane Home because of fever, dyspnea and epistaxis of 6 days' duration. After admission hematuria and hematemesis developed, and owing to a progressive increase in liver size and a rise in serum globulin concentration, a liver biopsy was done. Histologic examination revealed almost complete destruction of normal liver architecture, with eggs and adult worms of *Capillaria hepatica* everywhere evident. Postoperatively, it was found that the serum calcium concentration was only 5.2 mg. per 100 cc., although it had been normal on entry. Therapy in the form of vitamin D (50,000 units by mouth each day) was given for 3 days. On the 6th day after vitamin D had been discontinued the patient was found to have a serum calcium value of 20.3 mg. per 100 cc. (10.1 milliequiv. per liter). The serum "ionized" calcium was $>$ 8.0 mg. per 100 cc.[26]; the total protein was 11.8 gm., with 9.4 gm. of globulin, and the serum inorganic phosphorus 6.6 mg. per 100 cc. Seventy-two hours later the serum total magnesium was 1.13 milliequiv. per liter (0.63 milliequiv. per liter ultrafiltrable). Fifty-six per cent of the serum magnesium was ultrafiltrable. The serum calcium remained above 14.5 mg. per 100 cc. for the rest of the hospital stay. (Additional studies on the serum ultrafiltrable calcium of this patient have been published.[26])

Discussion

The data obtained on normal infants and children indicate that the total and ultrafiltrable magnesium of serum is maintained at concentrations no different from those found in the adult.

The present study, together with others,[14,15] failed to support the observations of Soffer et al.[11,12] and Dine and Laviettes[13] that the concentration of serum ultrafiltrable magnesium rises in hypothyroidism.

The greatly elevated values for total serum magnesium found in patients with chronic renal insufficiency are similar to the data obtained by Hirschfelder.[10] It should be noted that although the serum total value was three times the normal value in Case 4, the ratio of total to ultrafiltrable magnesium was maintained in a normal manner. Similar observations on serum calcium have been made by Hopkins and her colleagues,[26] who found normal ratios of total to ultrafiltrable serum calcium in most of their hypercalcemic patients.

The finding of an increase in serum total magnesium concentration immediately after death is reminiscent of the leakage of potassium from cells as a result of death or inhibition of glycolysis by fluoride or iodoacetate.[27] The present observations also seem to vitiate the report of Sunderman and Haymaker[28] who ascribed increased serum total magnesium concentration to other causes in an infant from whom the blood had been obtained after death.

The data obtained on a woman with idiopathic steatorrhea (Case 9) suggest a complete absence of protein-bound magnesium in her serum. The value of 0.29 milliequiv. per liter appears to be the lowest level for serum magnesium in a human being thus far encountered in the available medical literature. The patient was receiving a high-calcium diet and massive oral therapy with vitamin D. It is possible that the former factor, and perhaps also the latter, by favoring a relative increase of serum calcium concentration tended to promote a further decrease in serum concentration in a patient already depleted of magnesium by chronic steatorrhea. Such competition between calcium and magnesium in nutritional studies has been observed by Tufts and Greenberg.[29]

Case 10, the child with roundworm infestation of the liver, was practically hepatectomized, owing to the replacement of liver cells by nematode eggs and adult worms. It is hypothesized that the high levels of serum calcium observed were the result of lack of liver tissue for normal vitamin D storage; with even moderate vitamin D therapy the serum concentration of vitamin D should have increased enormously, this having an intensified hypercalcemic effect. Accordingly, it is suggested that in this patient, as in Case 9, the low serum magnesium concentration may have been in part the end result of an antagonism between calcium and magnesium.

Summary

Values for serum total and ultrafiltrable magnesium in a series of normal infants and children are described. The range of variation was narrow, with no changes of concentration with increasing age. The mean value for serum total magnesium was 1.77 milliequiv. per liter (standard error = 0.02); that for ultrafiltrable magnesium was 1.16 milliequiv. per liter (standard error = 0.02), and that for percentage of ultrafiltrable magnesium 65.3 milliequiv. (standard error = 1.8). These data are similar to those found in adults.

The study did not support previous findings that the concentration of ultrafiltrable magnesium rises in hypothyroidism.

Sharp increases of serum total magnesium were found in chronic nephritis, a normal ratio of total to ultrafiltrable magnesium being maintained.

Measurements of serum total magnesium in 2 children ante and post mortem demonstrated a significant elevation of serum magnesium immediately after death.

Two patients who showed diminished concentrations of serum total magnesium are described. Both had received massive doses of vitamin D. The possible relation of this therapy to lowered serum total magnesium levels is discussed.

Diminished serum magnesium concentrations in association with delirium tremens were recently reported by Flink et al.[30]

We are indebted to Drs. Lawson Wilkins and John Eager Howard, who made available patients from their clinics for this study, Drs. Theda R. Hopkins, David Baldwin and Barton Childs, who gave valuable aid, and to Mrs. Betty Lawrence for technical assistance.

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SPECIAL ARTICLE

HYPOKALEMIA ACCOMPANYING HYPERCHLOREMIC ACIDOSIS AFTER URETEROSIGMOIDOSTOMY*

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HYPERCHLOREMIC acidosis is not an unusual finding after ureteroenterostomy,[1] being noted in 79 per cent of 141 cases reported by Ferris and Odel.[2] Other investigators[3,4] describe a high incidence in patients whose ureters have been implanted into the bowel. There is still some difference of opinion about the relative importance of deranged kidney function versus intestinal reabsorption of urinary constituents in the pathogenesis of the electrolyte disturbance. Hypokalemia as an accompaniment of the disturbed electrolyte picture has not been widely reported, but it has been noted in scattered reports in the literature.[5-7] The low blood potassium level after ureterosigmoidostomy is quite compatible with chronically infected kidneys, although it may have other explanations, as pointed out below.

Case Report

A.R., a 34-year-old American waitress, was admitted to the Memorial Center for the 2d time on November 11, 1953, in a severe state of dehydration. lethargy and weakness. Her 1st admission was on January 30 with a diagnosis of basal-cell carcinoma of the cervix made by biopsy by her physician; previously, she had had menometrorrhagia for 6 months and some urinary frequency during the day and once or twice a night. Review of the systems was otherwise completely noncontributory, as were past and family histories. Physical examination during the 1st admission revealed normal vital signs, the only positive findings being a large, fungating mass supplanting the left half of the cervix and extending into the left parametrium. Biopsy demonstrated epidermoid carcinoma of the cervix, Grade 4.

Laboratory study showed a normal hemogram and a blood urea nitrogen of 9.0 mg. per 100 cc. Random urine samples were acid, with specific gravities varying from 1.011 to 1.018 and with no sugar or acetone. A faint trace of albumin was found on two occasions. Microscopical examination of noncatheterized specimens revealed 4 to 7 white cells, with 1 to 2 clumps of white cells, per high-power field. An intravenous pyelogram disclosed kidneys of normal size and shape, with prompt excretion of radiopaque material bilaterally. The ureters and calyxes were normal. The bladder demonstrated some indentation superiorly that was thought to be due to an enlarged uterus.

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On February 3 total hysterectomy, bilateral salpingo-oöphorectomy, total cystectomy, appendectomy and bilateral ureterosigmoidostomy were performed. Postoperatively, the patient did remarkably well, and the rectal drainage tube was removed on the 7th postoperative day. Six days later left costovertebral-angle pain and tenderness developed, with a temperature of 100.5°F. She was given 1.0 gm. of Gantrisin four times a day, and the pain gradually subsided over the next 3 days, but not before she had experienced some costovertebral-angle pain on the right side as well. An intravenous pyelogram on February 20 revealed beginning excretion at 15 minutes, continuing to 1 hour with ++ to +++ dilatation of the renal pelves and calyxes bilaterally. The ureters were not identified. Blood findings during this admission are recorded in Table 1. It is noteworthy that the blood urea nitrogen never exceeded 12.5 mg. per 100 cc. The patient was discharged to the outpatient department on the 19th postoperative day. Examinations in the outpatient clinic were unremarkable except for complaints of difficulty in rectal continence. She gained weight and felt clinically well.

On November 11 she presented herself in the clinic for a routine visit, and because of obvious dehydration and weakness, she was readmitted to the hospital. Her present illness had apparently begun 10 days earlier, when she first noticed what she thought was a cold, with coryza, malaise and weakness. She gradually lost her appetite and took less and less food during her illness. Two or three days before admission she began vomiting once or twice a day and passed more fluid by rectum than usual, although she was unable to estimate the increased losses. Four days before admission, she visited her physician, who prescribed an unknown amount of sulfanilamide.

Physical examination showed a lethargic, drowsy and weak woman, who responded to questioning only when physically stimulated to do so. She was thin, with a pale, dry skin with poor turgor. The mouth and tongue were dry. The fundi were normal. The lungs were clear to percussion and auscultation. The size of the heart was normal to percussion; the sounds were of good quality, and no murmurs were heard. There was no costovertebral-angle pain. The abdomen was soft and flat, with no palpable organs or masses. Bowel sounds were normal. Pelvic examination revealed a shortened vagina with no cervix, uterus or adnexa. Rectal examination was negative except for external hemorrhoidal tags. Deep tendon reflexes were present and equal bilaterally, and no pathological reflexes or sensory disturbances were noted.

The temperature was 99°F., the pulse 72, and the respirations 24. The blood pressure was 100/70.

Examination of the blood disclosed a serum sodium of 133 milliequiv., chloride of 128 milliequiv. and potassium of 2.5 milliequiv. per liter and a blood urea nitrogen of 39 mg. per 100 cc. An electrocardiogram showed a prolongation of the QT interval, with the T wave occupying almost the entire QT segment in all the standard leads[1] (Fig. 1). Drainage from an inserted rectal tube was not analyzed.

Intravenous fluid therapy was begun at 6 p.m. on the day of admission, and in the course of 36 hours the patient received 6300 cc. of fluids, which included 150 milliequiv. of potassium chloride, 135 milliequiv. of sodium bicarbonate, 500 cc. of 1/6 molar lactate and 200 gm. of glucose. Her clinical condition improved rapidly, and within 12 hours of the onset of therapy, she was alert and cheerful although still tired. Within 36 hours of admission, she was able to take a full liquid diet, including beef broth and fruit juices, without difficulty. On the following day she was placed on a soft diet and thereafter on a high-protein, high-carbohydrate diet. From the time she was able to take fluids by mouth her diet was supplemented in the form of tablets by 40 milliequiv. of potassium chloride (for 4 days only) and 23 milliequiv. of sodium bicarbonate up to and through the time of discharge. From the 4th hospital day until discharge the rectal tube was allowed to be removed during the day, with voluntary evacuations every 2 hours. The electrocardiogram returned to normal within 48 hours of admission.

Blood chemical values from day to day are listed in Table 2. It is noticeable that the blood urea nitrogen remained elevated throughout admission and that even on the day before discharge there was a tendency to hyperchloremia and acidosis. The patient was discharged on November 24 on a high-protein, high-carbohydrate diet, with 0.64 gm. of sodium bicarbonate 3 times a day (approximately 23 milliequiv.) and instructions to evacuate the bowel every 2 hours. Subsequent visits to the clinic revealed no recur-

TABLE 1. *Laboratory Data on the First Admission.*

DATE	CHLORIDE	CARBON DIOXIDE	SODIUM	POTASSIUM	BLOOD UREA NITROGEN
February	*milliequiv./liter*	*milliequiv./liter*	*milliequiv./liter*	*milliequiv./liter*	*mg./100 cc.*
2	104	27	138	4.4	9.0
5	97	28			9.0
9	94	27			5.7
11	99	27	134	3.90	4.3
18	111	23	140	4.01	12.5
21					11.0

TABLE 2. *Laboratory Data on the Second Admission.*

DATE	CHLORIDE	CARBON DIOXIDE	SODIUM	POTASSIUM	BLOOD UREA NITROGEN
November	*milliequiv./liter*	*milliequiv./liter*	*milliequiv./liter*	*milliequiv./liter*	*mg./100 cc.*
11	128	9	133	2.50	39
12	119	11	140	2.78	27
13	121	20	146	3.25	12
16	113	24	142	5.01	23
18	113	21	139	5.15	24
20	111	20	138	4.30	32
23	111	20	141	4.53	21

rence of symptoms of electrolyte imbalance although the tendency to hyperchloremia and acidosis persisted.

Discussion

The development of pyelographic abnormalities after ureterosigmoidostomy has been shown to occur in a large percentage of patients.[3,9,10] Lapides[3] reports a 77 per cent incidence of urographic abnormalities and electrolyte imbalance with a history of recurrent attacks of acute pyelonephritis in a series of 23 cases. Pool and Cook[9] describe a similar incidence of urographic abnormalities in a study of 43 patients within six months of operation.

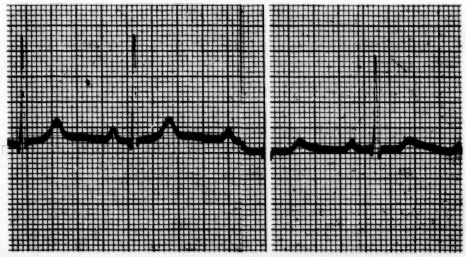

Figure 1. *Electrocardiograms (Lead 2) on November 11 (Left) and 13 (Right), 1953.*

Nevertheless, hyperchloremic acidosis has been shown to develop in patients who have no urographic evidence of damaged kidneys as well as in those who have, but with much less frequency in the former group.[10] Creevy and Reiser,[10] in a review of 111 patients who had undergone ureterosigmoidostomy, concluded that "hyperchloremia and acidosis were roughly 2½ times as common in the presence of gross bilateral renal disease, and produced symptoms more than 10 times as frequently as when one normal appearing kidney was present." They also suggested that more sensitive kidney studies might reveal a higher incidence of malfunction.

In the case reported above, it seems more than likely, in view of urographic abnormalities as well as the development of bilateral flank pain during the first admission and the persistently elevated blood urea nitrogen during the second, that some degree of kidney damage was present. One would be remiss in attributing this patient's hypokalemia to damaged kidney function alone, especially since such factors as vomiting, diarrhea and decreased food intake were also involved. Nevertheless, as mentioned above, hypokalemia after ureterosigmoidostomy has been reported. Diefenbach and his co-workers[7] report a case in which severe musculoskeletal symptoms developed to the point of flaccid quadriplegia. There was no associated history of nausea, vomiting, diarrhea or decreased food intake. Their patient responded dramatically to potassium and alkali therapy and was able to walk unassisted to the lavatory within an hour of the institution of therapy. The probable cause of the electrolyte disturbance was postulated as ascending urinary infection with resultant tubular damage and inability of the renal tubules to acidify the urine with secretion of potassium as a sodium-sparing mechanism.

Wilkinson[5] has also noted the occurrence of hypokalemia after ureterocolic anastomosis. Results of his investigations on 6 patients led him to suggest an increased "colonic secretion and perhaps hurried emptying of the lower ileum," with the consequent mild but chronic depletion of water, bicarbonate and potassium. He was not able, however, to distinguish between potassium secreted by the intestinal mucosa and that excreted by the kidney. He also pointed out that symptoms associated with hyperchloremic acidosis, in several patients in whom potassium levels had not been determined, were similar to those of hypokalemia, from which they may have resulted.

Foster, Drew and Wiss,[6] in a case report, attribute hypokalemia to decreased intake from intractable hiccuping.

Reports of hypokalemia in association with chronic renal disease are numerous.[11-13] Schoch,[11] in presenting 3 cases with a short review of the literature, concludes that potassium deficiency is frequent in severe chronic renal disease. Albright et al.[14,15] have reported several cases of renal acidosis or "tubular-insufficiency-without-glomerular-insufficiency." Their patients had high serum chloride with depressed values for carbon dioxide combining power, as well as hypokalemia. They suggest ascending infection of the tubules from pyelonephritis as a possible etiology, although in only 2 of their cases were urinary infections demonstrated. In 1 patient severe muscular weakness and paralysis developed before death, and although the serum potassium was not measured, in retrospect the authors consider it more than likely that it was low.

Burrows, Commons and Burnett[16] presented evidence of decreased ability of the diseased kidney to conserve potassium. They demonstrated nearly constant urinary concentrations of potassium in patients

with advanced renal disease after administration of varying solutions of electrolytes. Other investigators[17] reported similar findings.

The similarity between the patients of Albright and his associates[14,15] and those with hyperchloremic acidosis after ureterosigmoidostomy is striking. Both groups demonstrate elevated serum chloride with depressed carbon dioxide levels, and the symptoms after ureterosigmoidostomy are often compatible with potassium deficiency.

It is suggested that patients with hyperchloremic acidosis after ureterosigmoidostomy may have an impaired ability to conserve base, particularly potassium, in the kidney. The chronic loss of this electrolyte may compromise the large intracellular component of potassium so that any decrease in intake or excessive loss by vomiting or diarrhea may produce severe hypokalemia more rapidly than in patients with normal kidney function.

It is interesting that the patient described above, four days before the second admission, received an unknown amount of sulfanilamide, which has been shown to be a mild inhibitor of the enzyme carbonic anhydrase[18-20] that apparently plays an important role in the acidification of urine. Moreover, carbonic anhydrase inhibitors cause hyperchloremic acidosis, with an increased excretion of potassium.[21] Whether or not the sulfanilamide taken by this patient had any inhibitory effect on the carbonic anhydrase activity in any of the renal tubules cannot be determined, but it is an interesting speculation.

Summary

A case of hypopotassemia accompanying hyperchloremic acidosis after ureterosigmoidostomy is presented.

Some of the evidence favoring abnormal kidney function as a causative factor in electrolyte imbalance after ureterosigmoidostomy is reviewed. Previous reports of hypokalemia as a prominent feature of chronic renal disease and hypokalemia after ureterosigmoidostomy are noted, and the similarity in the two groups pointed out.

The suggestion that possible tubular damage after ureterosigmoidostomy may result in chronic potassium deficiency is made.

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MEDICAL PROGRESS

HYDRONEPHROSIS

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HYDRONEPHROSIS, a term originated by Rayer in 1841, is used to denote changes in the kidney that follow obstruction to the flow of urine. Because so many diseases in or adjacent to the urinary tract are capable of producing obstruction at various levels of the urinary channels, the condition is a very common one. This review is limited to a few of the discussions and observations over the years that have probed into the anatomic, physiologic, diagnostic and surgical aspects of the subject.

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Anatomic Observations

It is known that hydronephrosis may follow obstructive lesions anywhere in the urinary tract: proximally, from the level of the tubules in the kidney or the ureteropelvic junction, and distally to the external urethral meatus. The obstruction can be intrinsic, caused by abnormality, injury or disease within the

urinary channels; or extrinsic, occasioned by similar conditions adjacent to the channel. Obviously, a limited discussion cannot include the multitude of circumstances that have been described as interesting causes of hydronephrosis. This paper merely dwells on isolated studies that indicate progress along anatomic lines.

The Ureter in the Fetus and Newborn

A splendid study of the fetal ureter was reported by Östling in 1942. Two hundred and fifty fetuses at various stages of development were used for the investigation. In the embryo 4 or 5 cm. in length the ureter in the proximity of the renal pelvis was found to be narrower than the portion just distal at the level of the lower pole of the kidney. No kinks or folds were visible externally.

In the fetus of four or five months narrowing of the uppermost portion of the ureter was evident in most cases, with kinks held together by loose, transparent adventitia. In longitudinal sections the kinks appeared as muscular fold formations under the microscope, with axial offshoots of cell-deficient adventitia.

In the newborn infant a narrow part of the ureter was almost always observed just below the renal pelvis. Longitudinal folds were less pronounced, the wall being of the same structure as that in the wider areas of the ureter. However, by careful examination, Östling found superficial retractions in the inner part of the ureteral wall, corresponding to muscle folds in the incised ureter. Histologically, these areas consisted of parallel muscle layers, separated by outshoots from adventitia, the same composition as noted in the younger fetus. Exterior examination often did not reveal the narrowing of the lumen, but these areas were clearly demonstrated by means of casts of the ureter and renal pelvis.

The cause of physiologic differences in the caliber of the ureter is unknown, but these differences are prominent before any urinary secretion exists. This condition indicates that dilatations in the upper urinary tract of the fetus and newborn are signs of a disturbance in normal growth. Östling found dilatations of the upper urinary tract very common in the newborn and believed that they could not be considered as a mechanical hindrance. Histologic observations of the narrow ureteropelvic junction disclosed a normal muscular arrangement, occasional round-cell infiltration, but no inflammatory reaction. He concluded that the structure of the wall of the ureter at the site of narrowing rendered the congenital nature of the change obvious.

Varying degrees of external fixation in the region of the ureteropelvic junction were noted. Sometimes loose, sail-shaped adhesions were present; in others there was a firm membrane, which continued into the adventitia of the renal pelvis.

Although he observed that histologic changes in the ureteral wall were minimal, Östling expressed the view that the changes were congenital and probably physiologic; he also stated that these changes could at times be defined as an obstruction to urinary flow. The nonexistence of a muscular hypertrophy constitutes no proof that dilatation of the pelvis is not contingent on a remaining active hindrance to urinary outflow.

Östling's conclusions may be stated as follows. In every case of clinical hydronephrosis, one must take into account the possibility that a primary dilatation occurred in the early fetal state (without doubt because of disturbances in growth) and, further, that a secondary dilatation was caused by urinary stasis in postfetal life. He believes that the stenosis at the ureteropelvic junction has attracted too much attention and that the fixation of the ureter to the renal pelvis is the essential feature from the point of view of further development of hydronephrosis. As hydronephrosis develops, the more the kink or obstruction increases.

Östling found the so-called abnormal renal vessels not uncommon and supposes that these become more of an obstructive factor as the hydronephrosis enlarges and the kidney rotates.

Finding that the ureter is a relatively uniform tube up to the fourth month of pregnancy, Williams confirmed Östling's observations on the fetal ureter. After this period it discloses a differentiation into segments; however, there is no dilative manifestation. A narrow isthmus connecting to the renal pelvis is common.

Stenosis of Ureteropelvic Junction

Jewett has contributed a splendid study of the ureteropelvic junction in the adult, with histologic findings not unlike those described in the fetus. The examination of tissue from the ureteropelvic region of uninfected cases of stenosis at the upper end of the ureter, not complicated by aberrant vessels, showed the stenosis to be thin and delicate, the circumference of the ureter reduced and the epithelium and the muscular coat the same as in the pelvis and adjacent ureter, with no increase in circular muscle fibers to indicate a sphincter. It was necessary to conclude that the condition was congenital and that some factor in embryonic life interfered with development. As Jewett stated, "It is possible therefore that a ureteropelvic juncture represents a minimal narrowing which, when present in marked degree, becomes a congenital stenosis."

Aberrant vessels were noted in 34 of 43 cases studied by Jewett, but in 24 the obstruction caused by the vascular elements produced no intrinsic stenosis. Even in 10 cases in which both stenosis and abnormal vessels were present the stenosis was considered as the primary cause of obstruction for the following reasons: stenosis without vessels was observed three times as often as stenosis with vessels; the average age at onset of symptoms was thirteen years in those without vessels as compared to twenty-four years in those with vessels;

and the duration of symptoms was much shorter in those without vessels, indicating that it is unlikely that vessel contact produced stricture.

Hydronephrosis in Infants and Children

Campbell's comprehensive report on hydronephrosis in infants and children indicates that hydronephrosis is the most common abdominal tumor in this age group. His data were based on 828 cases (316 by autopsy and 512 by urologic study). Obstruction at the bladder outlet was a common cause in those with bilateral hydronephrosis. There was a high incidence of reduplication of renal pelves and ureters, the superior renal pelvis being involved in hydronephrotic changes twice as often as the lower pelvis.

Pathological observations showed the well known pelvicalyceal dilatation and parenchymal thinning, along with the sclerosis and destruction of secretory elements. The renal parenchyma became progressively compressed between the intrapelvic hydraulic mass and the dense renal capsule, interfering with the parenchymal blood supply and thus producing anoxemia and destructive cellular changes in the renal cortex.

Megaloureter

Recently, Swenson et al. presented a new concept concerning the etiology of the hydronephrosis and hydroureter found in the condition known as "megaloureter." It has long been known that megalobladder and megaloureters are often seen in cases of Hirschsprung's disease, or megalocolon. In 12 of 22 cases of megalocolon studied bladder capacity was larger than normal in all, and in 3 cases bilateral megaloureters were evident.

In megalocolon there is an absence of ganglion cells in Auerbach's plexus, a part of the parasympathetic pelvic innervation. It seemed reasonable to assume, therefore, that a group of patients with megaloureters and a bladder of large capacity might have a similar deficiency of nerve supply in the bladder or ureteral area.

In the normal bladder wall there is considerable uniformity in the number and distribution of ganglions in the adventitia, with greatest concentration near the entrance of the ureters into the bladder. In patients with megaloureter comparative observations disclosed diminution in number and variety of nerve cells and bundles in the bladder wall, although distribution was generally the same.

A study of 7 bladders obtained at autopsy by Swenson and his associates, in which the clinical picture was that of megaloureter and megalobladder, revealed a striking diminution in the number of ganglion cells in the bladder wall. There was no evidence of obstruction at the bladder neck in any, although the patients had large bladder residua.

Studies of ganglion cells in the ureters permitted no conclusions. Although the exact reason for malfunction of the ureters in these cases cannot be given it is believed that poor bladder function with a large quantity of residual urine leads to changes in the ureter because of either vesicoureteral reflux or back pressure without reflux. Evidence for this concept was shown by the improvement in the hydronephrosis and hydroureters after prolonged suprapubic drainage of the bladder.

Paraplegia

Talbot and Bunts have reported hydronephrosis in paraplegic patients in whom there was no evidence of stone. Of 331 patients observed over a period of two years 5 per cent showed hydronephrosis. In two thirds of those showing hydronephrosis vesicoureteral reflux could be demonstrated. The authors advised skin ureterostomy when the hydronephrosis is of such degree as to interfere with adequate renal function.

Dilatation of Collecting Tubules

Vermooten recently described a condition that he has named "congenital dilatation of the collecting tubules." In a review of 648 intravenous and retrograde urograms, the collecting tubules were visualized in 5 per cent. This disorder, most often noted in the intravenous studies, is not to be confused with pyelovenous backflow, which indicates stasis in the collecting tubules and a possible location of or inducement for stone formation. I have seen a patient whose tubular areas were visualized by intravenous pyelography with stone formation in several papillae of the kidney. The term "tubular hydronephrosis" might be used to describe this type of condition.

Summary

One may summarize these anatomic observations as follows: hydronephrosis may occur as the result of obstruction anywhere in the urinary tract and may be caused either by intrinsic or extrinsic lesions.

Studies of fetal ureters have revealed narrowing of the ureter at, or near, the ureteropelvic junction before the existence of any urinary secretion. This narrowed area is believed to be the result of a disturbance of normal growth. Varying degrees of external fixation have been noted with minimal histological changes.

Studies of the narrowed ureteropelvic junction in the adult have shown no histologic variation, and it was necessary to conclude that the condition was congenital.

Recent data have suggested that the hydronephrosis associated with megaloureters is sometimes caused by diminution of the number of ganglion cells in the wall of the bladder and disturbed bladder function. Hydronephrosis has been shown to develop in a small percentage of paraplegic patients and may be severe enough to warrant ureterostomy.

Congenital dilatation of collecting tubules may be an inducement to stone formation.

Physiologic Changes

When the excretory duct of the kidney (the ureter) is completely obstructed, a series of fascinating events ensues. Ligation or complete obstruction of the excretory duct of other body glands is followed by a primary type of atrophy. This primary atrophy does not occur when the kidney is similarly treated. Instead, hydronephrosis develops and hydronephrotic atrophy follows, except in rare cases in which blood supply is interrupted or cortical cellular activity is suddenly abolished. Why hydronephrotic atrophy occurs instead of primary atrophy is attributable to the reabsorption of contents from the renal pelvis, which thus permits further production of urine. This phenomenon of reabsorption and further urine production continues until the progressive effects of back pressure ultimately destroy all the functioning elements necessary for urine formation.

Various workers have demonstrated reabsorption of materials injected into the renal pelvis when the ureter is completely obstructed. Tuffier, in 1894, found that strychnine injected into the renal pelvis of a dog produced no sign of poisoning unless the ureter was ligated. Others have injected dyestuffs, drugs, bacteria and solutions opaque to x-rays into the obstructed renal pelvis to observe the same phenomenon of absorption. The material not only may disappear from the renal pelvis but also may be observable in the blood as well as in the urine produced by the opposite nonobstructed kidney.

Possible explanations for this physiologic event are as follows: absorption from the epithelial lining of the tract (mucosa of pelvis and calyxes), absorption via tubular structures of the kidney or absorption into the blood stream through a small traumatic area caused by distention.

Experimental Observations

Over the past two decades Hinman and his associates have presented many brilliant and detailed studies on the subject of experimental hydronephrosis that are worthy of review.

Observations on rabbits (which have a unilobed kidney) after ligation of the ureter demonstrated that high ligation favored a more rapid hydronephrosis than low ligation. As hydronephrosis developed the intrapelvic pressure forced the ampulla of the pyramid back and caused foreshortening and tortuosity of blood vessels, with diminished blood flow and partial anemia of the parenchyma.

In many hundreds of animals (rats and rabbits) complete ureteral ligation produced a primary atrophy only twice, and then in association with infection. Hydronephrosis of uniform degree, in proportion to time and in the absence of infection, was a constant finding. In other animals (dogs and cats) atrophy without hydronephrotic change was also rare. Hydronephrotic atrophy is believed to occur in man under similar circumstances. Partial obstruction of the ureter will in a longer time produce a much larger hydronephrosis than that which follows complete obstruction. No one knows if the activity of a hydronephrosis of certain size, caused by partial obstruction of the ureter, is similar to one of equal size, caused by complete obstruction, but on microscopical section of the kidney it is impossible to distinguish between complete and partial obstruction.

All workers are convinced that back pressure is the first essential factor in the production of hydronephrotic atrophy. The vascular changes are considered to be just as important as changes in cellular elements of the cortex.

The second essential factor in the development of hydronephrosis is the absorption of pelvic contents so that the excretory units continue to function. Experimental observations have found a gradual change in the composition of the contents of the dilating renal pelvis to demonstrate reabsorption and continuation of urine formation.

Hinman studied the various possible types of backflow or absorption. He reported that alkaline solutions promoted permeability of the hydronephrotic sac and that rats on a highly alkaline diet did not have hydronephrosis but died of "absorptive uremia."

Pyelovenous backflow, described by Hinman and observed in studies by Fuchs and others, pertains to the penetration of fluid from the renal pelvis into veins adjacent to the fornix of a calyx. It is established under a condition of back pressure. The phenomenon was reported in animals at intrapelvic pressures below the renal secretory pressure. Once backflow was established, it was found that the pressure required diminished as the hydronephrosis enlarged. The exact point of communication between the venous system and the fornix, however, is difficult to demonstrate, but it is believed to be distinct from extravasation.

Pyelovenous backflow occurred with considerable consistency in rabbits, sheep and man when ureteral injections were made into the pelvis slowly and with gradually increasing pressure. Pyelovenous backflow, as such, is not essential, however, to the development of hydronephrosis, because hydronephrosis occurs in kidneys of the chicken, alligator and frog, whose kidneys do not have papillae and fornices. In these animals extravasation takes place with rapid injection.

Tubular backflow is also a factor in the production of hydronephrosis. It is apparently produced easily in dogs but with difficulty in rats and cats. According to Fuchs it occurs more easily as time increases the size of the hydronephrosis. Material from the backflow must be taken eventually into the venous system, but the point of communication is again in doubt. The physiologic result, however, is tubulovenous back-

flow. Tubular backflow has been demonstrated by means of pyelography.

Observations in Human Patients

All types of reabsorption are believed to be possible in man. Fuchs produced pyelovenous backflow with intrapelvic pressure of 20-50 mm. of mercury in 70 per cent of his human kidneys. Certainly, the spreading open of a fornix and a minute tear into the venous channels, as well as into the sinus renalis, are possible with distention.

Narath studied the dynamics of the renal pelvis and calyxes, with graphic demonstrations by means of x-ray films, in man. After observing the activities of the calyxes and pelvis under normal conditions he studied the consequences for a brief period with the ureter suddenly obstructed. It was not possible to determine the intrapelvic pressure in addition to the pressure that the pelvis itself exerts to overcome the obstruction, but under conditions of acute obstruction, he believed it likely that pressure at the tip of the papilla and in the fornix of the calyx was higher than the secretory pressure.

Narath presented evidence that fluid from the pelvis can enter the canalicular (tubular) system, but he could only speculate whether this fluid is absorbed or expelled again as pressure subsides.

He believes that more significant absorption takes place by way of the fornix into the sinus renalis if excess intrapelvic pressure occurs. The mucosa of the fornix is said to be anatomically different from that at the neck of the calyx and has the ability of absorption under conditions in which there is no tear or injury that can be demonstrated. Observations were made of this process by a rise of pressure within the pelvis that was produced by the kidney and pelvis alone, and not by injection. Narath suggests as the proper term "fornical absorption," which is difficult to demonstrate by x-ray studies because of the rapid flow of blood in the capillaries and because of their tiny caliber. He believes that there can be both physiologic and traumatic absorption.

Rolnick and Singer, studying the effects of acute intrapelvic pressure in dogs, concluded that comparatively low pressure in the closed system of the kidney creates tears into the renal parenchyma, particularly at the poles of the kidney. Minor tears of the pelvic lining permitted dye to pass between the tubules into the intertubular spaces, from which it entered lymph and blood vessels.

Howarth recently presented 2 cases in man to demonstrate the insidious character of hydronephrosis after ureteral ligation. In each patient a period of over five years elapsed before symptoms developed.

Kretschmer discussed the consequences of ureteral ligation of the ureter in man and believed that hydronephrosis usually developed.

Partial Obstruction

So far, the discussion of physiologic changes has dealt with developments that occur in the completely obstructed kidney as far as these developments are known today. It is probable that the effects of partial obstruction are similar in many respects, at least so far as the anatomic pathology is concerned.

Partial obstruction is encountered far more often than complete obstruction in urologic problems, and it is therefore important to know about changes that follow release of obstruction to a hydronephrotic kidney. One might assume that removal of obstruction would permit renewed activity of the elements of the affected kidney, and this reactivation is true in most cases. However, under certain circumstances, permanent and significant functional activity may not resume even though sufficient renal tissue is available. This interesting phenomenon has been called "renal counterbalance" by Hinman.

Renal counterbalance has been defined as the anatomic and functional readjustment in the performance of total work required between the injured portion of renal substance and the less injured or uninjured portion. Evidence for the concept was accumulated from the experimental studies of Hinman and his associates. A hydronephrosis was produced by ligation of a ureter near the bladder. Later, at predetermined times, the ligated ureter was bisected just above the ligature, and the proximal portion was reimplanted into the bladder so that the hydronephrotic kidney could resume function. Several significant findings were observed. Mass hypertrophy was found in the kidney on the unoperated side when its mate was either removed or severely damaged by hydronephrosis. In adult animals the compensatory growth required twenty to thirty days and was noticeable particularly in the areas of glomeruli and convoluted tubules. Circumscribed hypertrophy was evident in the hydronephrotic kidney after release of the obstruction if need for its function were imposed gradually by interference with the function of the opposite good kidney. Functional compensation occurred much more quickly than anatomic compensation.

On the other hand, it was observed that when anatomic compensatory hypertrophy had occurred in the good kidney and this condition was maintained, the changes concerned with improved function of the hydronephrotic kidney were reduced to a minimum, and that these minor changes might even disappear in time. In other words, without the need for work by the hydronephrotic kidney, it failed to make significant recovery of function. There appeared to be an atrophy of disuse. However, for atrophy of disuse to take place, the hydronephrosis had to be severe and present for a long time.

Hinman et al. concluded that attempts to repair a unilateral hydronephrosis in the presence of complete compensatory hypertrophy on the opposite side were

always fruitless; the fundamental principles of compensatory hypertrophy and disuse atrophy must be considered. They found that there might be considerable initial recovery of function, but if the healthy kidney remained undisturbed, disuse atrophy followed months later in the hydronephrotic kidney.

These experimental observations and conclusions applied to clinical surgery mean that release of obstruction to a badly damaged hydronephrotic kidney would not necessarily be followed by improved function of that organ unless there were need of work for an adequate total renal function.

Further comment on this phase of hydronephrosis is made below in the section on surgical treatment.

Summary

One can summarize physiologic changes as follows. The kidney almost always develops hydronephrosis after partial or complete obstruction of its excretory duct (the ureter) rather than primary atrophy. Hydronephrosis takes place because of reabsorption of urine from the area of the renal pelvis and calyxes, permitting continued renal secretion until complete hydronephrotic atrophy occurs.

The routes of reabsorption are believed to be by pyelovenous backflow, pyelotubular backflow, from minute lacerations leading to venous communication adjacent to the calyx and perhaps by lymphatic channels.

Renal counterbalance deals with balance of function between the severely damaged hydronephrotic kidney and a kidney that has shown compensatory hypertrophy, on the basis of need for total renal function.

Diagnosis

The classic symptom of lumbar pain from hydronephrosis is well known, but the physiology of renal pain and its possible variations are often forgotten. Renal pain, except perhaps in the presence of acute inflammation, is caused by obstruction to the flow of urine from the kidney. The more acute and complete the obstruction, the more acute or violent the pain. The converse is also true. Less abrupt or partial obstruction causes less acute pain. If partial obstruction has been present since birth and has increased at an extremely slow rate the patient may be unable to recall any pain whatever, even though a large hydronephrosis is present. I have been able to demonstrate this actuality in physicians who were patients, as well as to physicians who were surprised that their patients had a large hydronephrosis with only minimal symptoms of discomfort. Of course, examination of the urine may be negative in all respects if no infection is present.

Aside from the characteristic pain in the kidney area as an indication of hydronephrosis, gastrointestinal symptoms are frequently the complaint that causes the patient to seek medical advice. Presumably, the symptom originates on a reflex basis or, if the hydronephrosis is large, on the basis of pressure.

Henline and Dawes emphasized this fact in a statistical survey of hydronephrosis by observing that 20 of 52 patients complained primarily of indigestion, flatulence or nausea. A normal urine specimen was common in their series.

Likewise, Lohrey, Poor and Osmond reported "stomach ache" of two years' duration in a seven-year-old girl whose diagnosis proved to be a large hydronephrosis on the left. In this case the urine was normal, and gastrointestinal studies were negative except for the extrinsic pressure on the stomach caused by the hydronephrosis.

The abdominal symptoms described above are common in patients with hydronephrosis. Certainly, the correct diagnosis could be arrived at with less delay if a plain film of the abdomen were routinely taken before x-ray examinations of the stomach and intestine and if intravenous urograms preceded the gastrointestinal studies. Experience demonstrates that several days are required to eliminate bismuth or barium from the gut, whereas dye from the urologic study is eliminated quickly, permitting prompt gastrointestinal studies.

The cause and diagnosis of hydronephrosis require pyelographic examination. One has to demonstrate the level of the obstructive process, as well as its nature.

Architecture of the pyelographic pattern has a normal variation just as the physical appearance of a person does. Robins and Fischmann called attention to this fact in an excellent paper describing three types of renal pelves,—intrarenal, intermediary and extrarenal,—as well as the changes produced on them by obstruction. They used the term "internal hydronephrosis" to designate dilatation restricted to the intrarenal portion of the drainage system of the kidney, a condition commonly seen in patients with intrarenal pelvis. A "combined hydronephrosis" involves both calyxes and pelvis and is most frequently seen in patients with an intermediary pelvis. The "external hydronephrosis" describes dilatation largely restricted to the renal pelvis.

McLaughlin and Bowler have reported a useful variation in intravenous urography for the demonstration of hydronephrosis. After the use of contrast mediums for intravenous pyelography the specific gravity of the urine may rise to 1.065. Therefore, urine containing the iodine compound will gravitate to the most dependent part of the urinary tract in which it is contained. These authors found improved delineation of the renal area by means of films taken at delayed intervals in the anteroposterior, posteroanterior and upright positions.

Engel, after a study of aberrant vessels as a cause of hydronephrosis, decided that a kettledrum type of hydronephrosis in an extrarenal pelvis with opaque medium sharply confined to the pelvis was a typical diagnostic feature of the condition.

One of the newer diagnostic aids in urology is the delineation of the vascular tree by aortography. As mentioned above, an advanced hydronephrosis interferes with cortical blood supply. Adequate blood channels are necessary for proper function of the nephrons. Therefore, if the vascular pattern of the kidney can be visualized, some idea of its potential capabilities can be obtained. These findings could influence a decision whether the hydronephrotic kidney might be salvaged by plastic repair or had better be removed.

Doss, who has had a large experience in this method of examination, believes that the ordinary older methods of determining renal function should not be relied on exclusively. He regards the condition of the arterial tree in each kidney as determining whether the organ should be preserved or removed. He also has found translumbar aortography a good method for establishing the relative over-all status of the kidneys. Excluding tumors, a good cortical blood supply to a kidney should indicate conservative surgery, whereas occlusion of the main arterial tree, appreciable reduction in the number of larger intrarenal vessels or absence of smaller intrarenal vessels indicates nephrectomy.

Smith and his associates have also had an extensive experience with translumbar arteriography. They have shown graphically how replacement of normal renal parenchyma by hydronephrosis decreases the arterial circulation of the kidney. In a review of 200 translumbar arteriograms an anomalous renal artery was demonstrated in 9 cases as the cause of the hydronephrosis.

In summarizing the progress of the diagnostic methods as they pertain to hydronephrosis one must certainly be alert to the fact that the degree or severity of flank pain may be minimal in the presence of advanced disease and that abdominal symptoms may be the most prominent feature. The aim of diagnostic tests is to determine not only the location and nature of the obstruction but also the potential integrity of the remaining kidney tissue. For an accurate appraisal of the situation, it will be necessary to use intravenous urography, retrograde pyelography, various renal-function tests and perhaps visualization of the renal circulation. Information regarding the opposite kidney is just as important as data about the organ under suspicion.

Surgical Treatment

Since the cause of hydronephrosis is obstruction, the cure necessitates either removal of the obstruction or removal of the kidney by surgical means. This discussion is limited to concepts and procedures dealing with obstruction at the level of the ureteropelvic junction.

The decision whether to resort to reconstructive operation or nephrectomy depends on the age, general condition, activities and occupation of the patient, the potential functioning capacity of the kidney in question and the presence and condition of the opposite kidney. All judgment should be on the basis of individual consideration.

Conservative renal surgery is a term used repeatedly today. As a procedure this is laudable but not so new as one might suppose. Fifty or more years ago surgeons had the same ideas and ambitions. For instance, in 1908, Watson and Cunningham, wrote: "The chief principle to be observed in the surgical treatment is that of employing one or another of the conservative operations whenever possible. . . ."

Conservative renal surgery for the relief of hydronephrosis entails eliminating the obstructive factor and retaining the kidney as a functioning unit. According to Berneike and Deming, the criteria of success for this type of surgery are fourfold: relief of symptoms, improvement in function, disappearance of infection and disappearance of dilatation.

Many surgeons have proposed surgical technics to accomplish the desired result. They vary in principle or in details of modification. However, they may be grouped into six types with the realization that one or more types may be utilized in one patient:

Pyeloureteralysis refers to the freeing of fibrous bands or adhesions, or the severance of a small aberrant vessel in the region of the ureteropelvic junction. The aim is to relieve extrinsic obstruction and permit the free flow of urine through this area if there is no intrinsic factor.

Incisions at or near the ureteropelvic junction, with closure, as suggested by Heineke and Mikulicz and Fenger, or incision into the dependent pelvis and adjacent ureter with closure by anastomosis, as proposed by Finney, attempt to provide a better outlet for urine from the renal pelvis by increasing the diameter of the stenosed area.

A V-type area from the renal pelvis, which is moved into the stenosed region by means of a so-called Y plastic procedure, as described by Schwyzer and by Foley, has often proved successful. A tongue-flap type of plastic procedure, utilizing the wall of the renal pelvis, has also been described by Culp and DeWeerd as being adaptable to the narrow ureteropelvic junctions that are dependent. It is claimed that this procedure increases the diameter of the involved ureter without producing angulation at the base of the flap.

An operation attempting to mold the kidney into a ball-like shape was described several years ago for use in cases of hydronephrosis caused by an aberrant artery at the lower pole. Stewart stated that he hoped to change the shape of the kidney by bringing the two poles together so that the aberrant artery could come into close relation with the renal pedicle and hence cease to be an obstructing agent. The kidney was held in its new shape by a hoop of surgical-gut tape and by sutures in kidney tissue and capsule, thus approxi-

mating the anterior surface of the upper and lower poles. Stewart reported 18 cases so treated. The operation has not, to my knowledge, been accepted with enthusiasm.

Bisection of the ureter with resection of a short stenosed area, followed by reimplantation of the ureter into a dependent portion of the renal pelvis, has been used with success by some surgeons, especially in cases in which an aberrant artery is too large for ligation without danger of infarction. Berneike and Deming presented a convincing report of a series of 30 patients who had been thus treated.

Linear incision through the wall of the stenosed segment, followed by splinting with the largest possible tube, and without attempt at closure of the incised ureter, has been advocated, especially by Gibson and Davis. Davis has called the procedure "intubated ureterotomy." After this type of operation the ureter grows over the splint and ultimately should have a diameter of normal caliber. Gibson regards splinting or intubation as more important in obtaining a good result than the most meticulous suturing.

Davis, Strong and Drake have reported experimental work on regeneration of the ureter. Two thirds of the circumference of the ureters of dogs were excised; the ureter was intubated, and the kidney above removed. At the end of six weeks the circumference was completed by connective tissue said to be capable of peristalsis, and muscle had surrounded three fourths of the circumference. As Henline pointed out in the discussion of this work the repair process has been shown to occur in a normal ureter, rather than in a strictured or fibrosed ureter.

Davis describes the advantages of intubated ureterotomy with the assertion that the operation is applicable to all cases, regardless of the location, length or multiplicity of the strictures. It is a simple procedure. There is no dependence for success on a suture line. The splinting tube can be left in place as long as the surgeon desires so that good results may be obtained even in the presence of infection.

From the multiplicity of surgical procedures set forth it is obvious that no operation is necessarily adaptable for all types of obstruction at the ureteropelvic junction, nor is any procedure universally successful. O'Conor has emphasized this opinion after review of his own cases.

There are currently two distinct points of view about the advisability of splinting the operated segment of ureter. Deming, with his meticulous technic, obtained excellent results without a splint through the operated section, although, when it was necessary to resect the ureteropelvic junction and anastomose the ureter to the dependent pelvis, a ureteral T tube was used as both a splint and a drain. As mentioned above, other urologists believe that the ureteral splint is essential to the success of the operation.

Drainage of the kidney by nephrostomy or pyelostomy is necessary during a period of splinting and is also advisable in the plastic type of repair, especially if urinary infection is present at the time of surgery. Drainage prevents tension on sutures by avoiding distention of the repaired area, permits adequate urinary output and allows pyelography through the tube for observation of the probable result.

When one reviews the published clinical results of various authors using one or more of the various surgical technics it is apparent that most of them report 85 to 90 per cent "satisfactory results" and 10 to 15 per cent failures. Thus, nature defies man's best intent at some statistical level.

Conclusions

To summarize progress in the surgical treatment of hydronephrosis, one must first evaluate the degree and probable cause of the condition. If the change is minimal, it may be advisable to postpone operation and have periodic study to ascertain whether the condition is static or progressive. There should be a definite indication for surgical interference either by symptoms or by pyelographic evidence before one proceeds with operation. The condition of the opposite kidney often influences the advisability as well as the type of operation that is best in the particular patient.

In general the decision for reconstructive surgery, rather than nephrectomy, will be favored if it is estimated that an uninfected, hydronephrotic kidney is capable of performing one quarter or more of the total renal function. That amount of renal tissue would sustain life if the opposite organ met with serious misfortune. The physical and economic drain on the patient will, of course, be longer than that after nephrectomy.

The type of plastic repair to be used will be influenced by the kind of problem at hand and by the success of certain operations in the experience of the particular surgeon. It should be remembered that in the success of any surgical procedure, the surgeon is just as important a component as the method that is being employed. No doubt with the idea of renal counterbalance in mind Hinman once wrote, "This policy of surgical repair so boastfully endorsed by many shows operative skill only without understanding or judgment of renal physiology."

Nephrectomy may well be the best operation if there is little renal tissue left and if the opposite kidney is sound.

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MEDICAL INTELLIGENCE

TRICHO-X-RAY CANCER

Another Case of Radiation-Induced Tumorigenesis

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THE property of radioactivity that characteristically enables it to alter normal biologic, biochemical and physical behavior renders its use extremely hazardous. Cellular injury results when a low tissue threshold for radioactivity is exceeded, when tissues are exposed to excess radiation or when lesser exposure is rendered for a prolonged period.

Radiation damage is capable of affecting all cells; however, the consideration of its effects is limited, in this paper, to those involving the skin. Acute or chronic radiodermatitis is the most frequent effect of irradiation. The acute phase is characterized by a progression of inflammatory change manifested as erythema, vesiculation, desquamation, brawny edema or necrosis, or all five. The chronic manifestations are pigmentation, depigmentation, telangiectasia, cicatrix, wrinkling, atrophy, keratosis, ulceration and neoplasia. These changes, significantly, occur many years after the initial exposure. Greeley[1] has observed ulceration or cancer that developed as late as fifty years after exposure.

Radiation-induced tumorigenesis is a familiar sequel previously witnessed in the epitheliomas and leukemias that developed in radiologists and others working without adequate protection from roentgen rays and radium. More recently, leukemias and other radiation-induced cancers were seen in the late survivors of Hiroshima. Furthermore, radiation cancers have been reported in the skin,[2] bones,[3,4] uterus[5,6] and breast.[7] MacKee and Cipollaro[8] have observed cancer developing in an estimated 25 per cent of patients with radiodermatitis, particularly of the chronic type. These cancers are usually of the squamous-cell type, although basal-cell, sarcomatous and Bowenoid lesions have been reported.[8] Doubtless more radiation cancers would be seen if cutaneous radiation injuries were not effectively treated by surgical means before the onset of malignant degeneration.

Radiation-induced tumorigenesis is tragic when it is a result of the indiscriminate use of x-rays or radium

and, more particularly, when it is the result of injudicious application in the treatment of benign conditions. The "tricho" treatment for the removal of superfluous hair is a case in point. The tricho system, which was invented by Albert C. Geyser, M.D., of New York City, consists of exposing the treated part

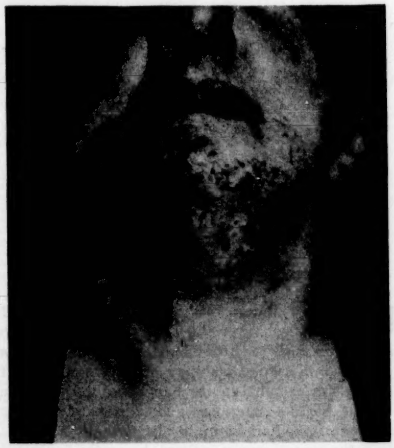

FIGURE 1. *Previously Irradiated Site Characterized by Atrophy, Telangiectasia, Pigmentation and Malignant Ulcer.*

to a machine allegedly issuing short vibratory waves (0.3 of an Angström unit) intended to dry up the dermal papillae. A booklet issued by the system states that the apparatus and technic of its operation have

FIGURE 2. *Close-up View of Figure 1. Note the extreme degree of chronic radiodermatitis and squamous-cell carcinoma.*

been examined and endorsed by many leading physicians. It further states that the attitude of the medical profession is illustrated by the fact that tricho treatments have been given to the wives, daughters and sisters of physicians. A ten-point summary of the publication includes the following:

1. Tricho system removes superfluous hair permanently.
2. No scars or other injury to the most delicate skins.
3. Endorsed by physicians and beauty experts.
4. Scientific — safe — sure.
5. Permanent removal of superfluous hair guaranteed.

This report and others previously published constitute evidence that the tricho treatment is neither safe nor scientific, but rather that it is extremely hazardous and capable of producing malignant degeneration. Cipollaro and Einhorn[9] reported 4 cases of chronic radiation dermatitis and epitheliomas occurring in females twenty to twenty-five years after tricho x-ray

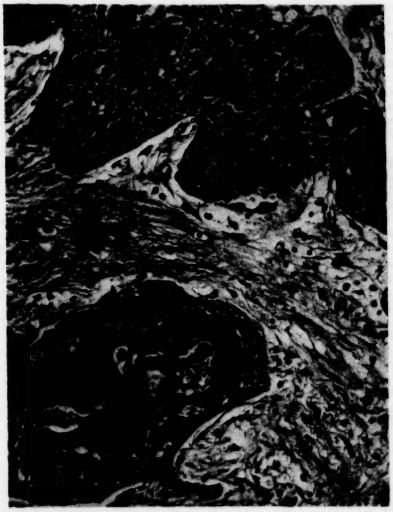

FIGURE 3. *Photomicrograph, Showing a Nest of Infiltrating Cornifying Squamous-Cell Carcinoma. Note the hyperchromatic nuclei and mitotic figures.*

treatment for superfluous hair. Fox,[10] Oliver,[11] Lane,[12] Silver[13] and others[10,14-16] have recorded cases of chronic radiodermatitis after tricho exposure. Kaplan[17,18] described a case of epithelioma of the cheek fifteen years after this treatment, and a case of fibrosarcoma of the cheek seven years after therapy.

CASE REPORT

M.S., a 58-year-old spinster, was first seen on September 2, 1953, because of an indurated ulcer of the chin. This lesion was alleged to have been present for 3 years, with occasional crusting but with incomplete healing. She stated that in 1914 she began having electrolysis for the removal of superfluous hair. These treatments continued every other Sunday for a total of 50 treatments. In 1923 she began tricho treatments once a week for approximately 5½ months. This

entailed about 24 sessions at a cost of $10 each. After the last treatment she noted pigmented "spots" about the chin and neck. These were exaggerated by exposure to sunlight. Permanent discoloration, however, did not appear until 1930.

Physical examination revealed an indurated ulcer, 2.5 by 1.5 by 0.8 cm., overlying the symphysis mentis and fixed to the underlying mandible. Scattered over the skin from the mid-thyroid cartilage to the vermilion border of the lower lip and the angles of the mouth laterally was an area of atrophy, telangiectasia and light and dark brown pigmentation, 12 by 8 cm. (Fig. 1 and 2). Examination of the neck revealed a thickened indurated skin and subcutaneous tissue but no palpable lymph nodes.

X-ray examination of the mandible showed a small area of absorption underlying the ulcer, and neoplastic infiltration could not be ruled out. A film of the chest was normal.

Biopsy revealed ulcerative squamous-cell carcinoma.

On September 18, under endotracheal nitrous oxide, oxygen and ether anesthesia, a wide excision of the ulcer was performed. This excision involved the mucous membrane of the lower lip and the cortex of the underlying mandible. A 2d incision was made in semicircular fashion extending from the mastoid processes to thyrohyoid membrane. The subcutaneous fat was noted to be dark brown and matted, in contrast to normal lobulation. A modified suprahyoid neck dissection was done, and the mandibular defect was closed by elevation of the cervical flap. The cervical incision was approximated without tension and permitted primary suture. Two drains were inserted. The cutaneous flap and mucous membrane were approximated with interrupted sutures. Healing was uneventful.

Microscopical examination revealed cords of neoplastic cells extending into adjacent corium and striated muscle, with frequent hyperchromatic nuclei and mitosis (Fig. 3). The bone and periosteum were free from tumor, and all the lymph nodes were negative for tumor cells.

The patient had an uneventful convalescence, and on September 23, a double pedicle was raised from the anterior part of the thoracic wall and resutured. This was tubed on October 2. On November 23 the cervical mandibular flap was resected, and the pedicle flap was raised to cover the defect and re-form the chin. A head-and-body cast was applied to prevent stretching of the pedicles. Microscopical examination of the submitted specimen showed atrophic chronic dermatitis consistent with postradiation dermatitis. The epithelium was pigmented and atrophic and showed a loss of the rete pegs. The dermal adnexas were absent, and the elastic tissue of the corium was replaced by collagen. In other sections the epidermis was moderately thickened. The sudoriferous glands were hyperplastic and surrounded by mononuclear cells.

On December 28 the flaps were severed and the final plastic procedure performed.

Conclusions

This and other cases of radiation-induced tumorigenesis attest to the tragic outcome of the indiscriminate and injudicious use of radiation therapy, particularly for benign conditions. The best method of treatment of radiation cancer is its prevention.

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DOCTORS AFIELD

Nicolaus Coppernic (1473–1543)

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THE only definitive biography of Copernicus — that by Leopold Prowe[1]—is not approved by Polish patriots, because it honors him as a great Prussian rather than as a Pole. He was born in Thorn, an East Prussian city founded by the Knights of the Teutonic order, of Silesian parentage, and (fortunately) wrote only in German and Latin, but he certainly acknowledged the sovereignty of a Polish king. Copernicus is celebrated, however, not for being a Silesian, Prussian or Pole, but as the elaborator (with the probable aid of no instrument other than a home-made wooden triquetrum) of a new heliocentric astronomy.

At the age of eighteen he matriculated at the "University" of Cracow in 1491, one of a class of 218 freshmen. Here, he read the Latin classics and was introduced to arithmetic, Euclid and astrology. When he was twenty-three years old, he journeyed to Italy, where for four years he studied the civil law at the University of Bologna. The next four years he devoted to the study of canon law at Padua. In 1503 he received his doctor's degree at Ferrara. He then took up the study of medicine, which occupied him for three years. In 1506, at the age of thirty-three, he returned to Heilsberg, in Ermland, to live with his uncle, Lucas Watzelrode, the bishop, whom he served as political and administrative assistant. In the summer of 1512, after the death of his uncle, he moved to the cathedral town of Frauenburg, where he spent the rest of his life as a canon and deputy of the bishop. He never assumed ecclesiastical orders. A tower in the northwest corner of the cathedral square was the observatory used by Copernicus for his astronomical studies.

An early biographer, Starowolski, records the tradition that Copernicus was celebrated in Frauenburg as another Aesculapius. Gassendi, writing a hundred years after Copernicus's death, says that he never en-

gaged in the public practice of medicine. His actual practice, although probably more or less continuous and active, seems to have been confined to treating the ailments of various distinguished members of the reverend clergy.

His medical library, together with his other books, is preserved in the library of the University of Upsala, where it was removed by Gustav Adolph after his campaign against Sigismund III of Poland during the Thirty Years' War. What appears to have been one of Copernicus's favorite prescriptions is reproduced in Figure 1. A translation is as follows:

boli armenici	(Armenian bole)	2 oz.
cinamomi	(cinnamon, or cassia)	½ oz.
zeduarii	(zedoary)	2 dr.
tormentillae radicis	(tormentil)	
diptamni	(fraxinella)	
sandalorum rubrorum	(red saunders, or sandalwood)	of each, 2 dr.
rasurae eborum	(scrapings of ivory)	
croci	(tree saffron)	
spodii	(ashes)	
anthemii (?) acetosi	(camomile)	of each, 2 scruples
corticis citri	(lemon peel)	
margaritarum	(pearls)	of each, 1 dr.
smaragdi	(emeralds)	
iacinti rubri	(red hyacinth)	
zaphiri	(sapphires)	of each, 1 scruple
os de corde cervi	(bone of stag's heart)	1 dr.
carabae	(lobster ?)	
cornu unicorni	(unicorn's horn)	
coralli rubri	(red coral)	
auri	(gold)	
argenti tabularum	(silver leaf)	of each, 1 scruple

zuccaris (sugar) lib. s. vel quantum sufficit. fiat pulvis

This prescription, which is found in many old pharmacopeias, is copied on a flyleaf of Copernicus's volume of Euclid's *Elementa Geometrica.* Armenian bole is a ferruginous aluminum silicate. Pearls and coral were a source of calcium carbonate. Emeralds and sapphires provided aluminum oxide. Ashes furnished alkaline carbonates, and unicorn horn (or hart's horn) calcium and ammonium phosphate. Cinnamon, zedoary, fraxinella, tormentilla and hyacinth are vegetable astringents. The mixture may sound fantastic, but is not irrational. The same prescription is found on a flyleaf of his volume of Petrus de Largelata's *Chirurgia.* A number of other clinical notes indicate his constant interest in the practice of his profession.

The spelling of Copernicus's name has been seized upon by supporters of one or another "national" origin of his name and family as a suitable matter to squabble about. When he wrote informally, the great prebendary-physician-astronomer himself always used the form Coppernic; in his formal writings he latinized his name into Coppernicus. On the title page of the first printed edition of *de revolutionibus orbium caelestium* the author's name appears as Copernicus. (One p hints that the name is derived from a Polish word meaning dill, as in dill pickle; two p's suggest the Low-German word for copper.)

Copernicus never found it necessary to confuse his religion with his "hypotheses" (as they were cautiously termed by his publisher), but he was ridiculed during his lifetime for his revolutionary ideas by both Martin Luther and Philipp Melanchthon. *De Revolutionibus* was not placed on the *Index* until seventy-three years after his death, subsequent to the Galileo hassle.

The printed book, *Concerning the Revolutions of Heavenly Bodies,* did not appear until Copernicus was on his deathbed. This delay in publication (his ideas had probably been formulated at the period of his return from Italy in 1506, and were in circulation

FIGURE 1. *A Prescription in the Handwriting of Dr. Nicolaus Coppernic (Reproduced from Prowe[1]). The signature is reproduced from a folio volume preserved in the University Library at Upsala.*

among his learned contemporaries at least as early as the year 1533) is explained in his dedication to Pope Paul III:

> I have debated with myself whether to print [my new theory of the motion of the earth] or whether it were better to follow the example of Pythagoras and others, who transmitted the mysteries of their philosophy not in letters but by word of mouth, and only to their adherents and friends.

It is regrettable that no adequate biography of Nicolaus Coppernic exists in English. The two-volume life by Prowe,[1] as well as the biography by Mizwa,[2] is in the Boston Public Library.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 40221

PRESENTATION OF CASE

First admission. A forty-nine-year-old lawyer entered the hospital because of a lesion in the lung.

Ten years previously he had an attack of myocardial infarction; an x-ray film of the chest at that time was normal. Since then, he had had routine checkups of the heart every six months but without x-ray examination. About six weeks before admission, a lesion was noticed in the left lung on fluoroscopic examination. There was no history of cough, expectoration, hemoptysis or chest pain.

Ten years before admission he had been a heavy smoker, but he had not smoked since the myocardial infarction. An appendectomy had been performed thirteen years before admission. He had had several attacks of gout, the last of which occurred three years before admission. His mother had a breast cancer but was living at the age of seventy-two years; the father had died of a cerebrovascular accident at fifty-four years of age. There was no history of tuberculosis.

Physical examination revealed no abnormal findings.

The temperature was 99.5°F., the pulse 100, and the respirations 22. The blood pressure was 145 systolic, 85 diastolic.

Routine examination of the blood and urinalysis were negative. Roentgenograms of the chest showed, at the left hilus and extending outward chiefly posteriorly toward the superior segment of the left lower lobe, an ill defined density measuring 4 cm. in greatest dimension (Fig. 1 and 2); the left bronchial tree was visualized to the orifice of the left upper lobe, but the lower-lobe bronchus was not as well seen as in normal subjects and there was a definite suggestion of a mass encroaching on the lumen immediately below the origin of the upper-lobe bronchus. No evidence of mediastinal shift or change in diaphragmatic motion was observed on fluoroscopic study; the esophagus was not remarkable, and no definite mediastinal lymph nodes were seen. Bronchoscopic examination, however, was negative, and a smear of the bronchial secretion demonstrated no acid-fast bacilli; cytologic examination was unsatisfactory. The patient was discharged and advised to return in a month for further study.

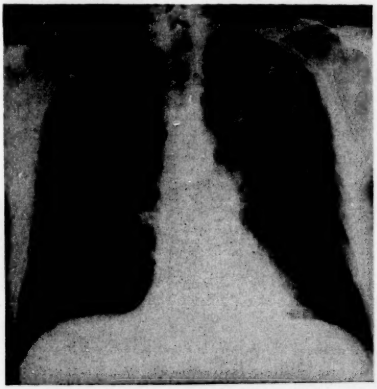

FIGURE 1. *Roentgenogram of the Chest.*
Arrow points to abnormal density within the apical segment of the left lower lobe.

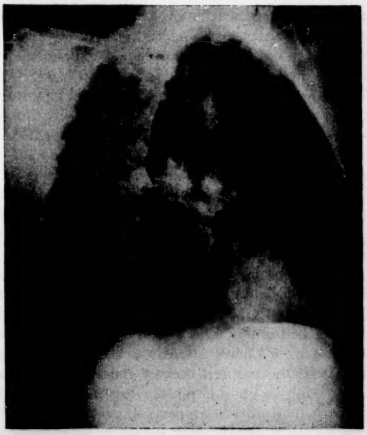

FIGURE 2. *Right Anterior Oblique Roentgenogram of the Chest.*
The abnormal density within the apical segment of the left lower lobe is indicated by arrows.

Second admission (six weeks later). A month after discharge a repeated chest roentgenogram revealed that the density appeared better defined and slightly larger, but there was no definite intrabronchial extension. The patient was readmitted to the hospital for operation ten days later.

The physical findings remained negative.

The temperature was 98°F., the pulse 80, and the respirations 20. The hemoglobin was 15.1 gm. per 100 cc., and the white-cell count 4200, with 61 per cent neutrophils.

Two days later an operation was performed.

Differential Diagnosis

Dr. Joseph Hanelin*: The problem presented by this patient is frequently encountered by the radiologist. We are confronted with a relatively healthy patient who had been found to harbor an abnormal density in the lung. He had been investigated clinically and subjected to bronchoscopic examination, and his bronchial secretions had been examined, all with negative results. After a short period of observation, six weeks in this case, the lung density persisted without great change. Should he have been observed further or explored surgically? It was decided, I think wisely, to do a surgical exploration, with the thought in mind, of course, that an asymptomatic bronchogenic carcinoma may have been present and the sooner it was removed the better.

The available films cover a period of approximately six weeks. When the patient was originally seen the abnormal density described in the protocol was observed overshadowing the left hilus. It has rather poorly defined margins except for the lateral, inferior portion, where it is more sharply demarcated; it is about 5 cm. in greatest dimension. It is best uncovered in the right anterior oblique view, where it is shown to lie posterior to the hilus and is situated within the apical segment of the left lower lobe (Fig. 1 and 2). There is a suggestion of minimal subcarinal adenopathy, but this is not definite. I cannot be certain of any encroachment on the bronchus of the left upper or lower lobe. The esophagus follows a normal course through the mediastinum. Four weeks later the density is slightly larger in the frontal projection but is more sharply demarcated laterally. Another examination two weeks later shows persistence of the lesion, not greatly changed, although it now appears slightly smaller, particularly in comparison with the right anterior oblique views. Early lesions in this particular location are often overlooked, being mistaken for prominent vessels; it is also true that prominent vessels in this region may be mistaken for early evidence of neoplastic disease. There seems to be little question, however, in this case that there was some abnormal process within the lung parenchyma.

*Associate radiologist, Massachusetts General Hospital.

A variety of lesions present themselves for consideration in the differential diagnosis, both neoplastic and non-neoplastic. Primarily, the problem is to differentiate, if possible, a primary bronchogenic carcinoma and an inflammatory lesion. The precise duration of the process is uncertain.

A word might be said about pulmonary infarction. This location is uncommon for an infarct, which is more frequently situated in the basal portion of the lower lobe. An infarct of this size tends to disappear in several weeks unless secondarily infected, leaving a linear or stellate scar. Infarcts may on occasion be clinically silent, but if infection supervenes, definite clinical manifestations are present. I shall exclude infarction.

Could this have been a primary bronchogenic carcinoma? Radiographically, it is impossible to exclude that possibility. Despite the negative bronchoscopic examination tumor may well have been present within the apical bronchus and may have occluded it distal to its proximal orifice so that it was not visualized. Much of the density within the apex of the lower lobe with its generally irregular margin, I should expect, would then have represented atelectasis and pneumonitis peripheral to an occluded bronchus. The tumor itself would not be distinguishable from the adjacent changes in the lung. The presence of unequivocal adenopathy would help me to make this diagnosis, although, of course, adenopathy could be present with an inflammatory lesion as well. The changed appearance of the density over the six-week period is somewhat against the diagnosis of neoplasm, particularly the suggestion that the density had contracted, but that by no means eliminates it, because pneumonitis peripheral to an occlusion may become larger and smaller from time to time.

A word might be said about pulmonary adenomatosis, which I think can be excluded. Initially, it may manifest itself as a patch of density in a single lobe; it tends, however, to spread rapidly in the lung both on the same side and contralaterally. Many authorities believe that it has a multicentric origin. Frequently, when the patient is first seen, there is bilateral pulmonary disease. Usually, there is a cough, which is often productive of large amounts of mucoid sputum.

A metastatic carcinoma to the apical bronchus might be mentioned; however, there was no known extrathoracic lesion and no real basis exists for considering this possibility.

A bronchial adenoma, of the carcinoid type, could conceivably have caused these changes by obstructing the apical bronchus. This lesion is more common in females, generally has a longer duration and usually manifests itself by intermittent hemoptysis or pulmonary infection or both.

I shall dismiss a foreign-body reaction in the absence of a history of foreign-body aspiration.

I am left with the group of inflammatory lesions. The only evidence of infection was the single recorded

temperature of 99.5°F. I should be interested to know if careful questioning disclosed a history of upper respiratory disease that was not mentioned in the protocol. I dismiss lipoid pneumonia due to mineral-oil aspiration on the basis of both the negative history and the location of the process. Most commonly this is present in the basal segments of the lower lobe; it is frequently more diffuse and patchy, and is likely to involve the right lower lobe.

Could this have represented a chronic pneumonitis of the cholesterol type described by Robbins and Sniffen[1]? Chronic cholesterol pneumonitis may have either a lobar or a segmental distribution. It lies against at least one pleural surface and may or may not contain small cavities. Its margins are lobulated, and usually sharply demarcated. All the 11 cases discussed in their paper gave clinical evidence of either acute or chronic respiratory disease, and the lesions were all larger than the one in the case under discussion.

Tuberculosis must also be borne in mind, although nothing substantiates this diagnosis. In its favor is the fact that tuberculosis occasionally involves the apex of the lower lobe, and this localization has been noted in a number of patients in this hospital. We have no reason to suspect other infections of bacterial, fungous, viral or rickettsial origin on the basis of either laboratory or clinical evidence.

An unresolved or slowly resolving interstitial pneumonia is a distinct possibility. Clinically, its manifestations may not be marked; ambulatory pneumonia is not uncommon although these people generally have some symptoms. There was evidence of slight fever when the patient was first seen, and the process had cleared somewhat in the two weeks before operation. Generally, interstitial pneumonia is of viral etiology although it may also be of bacterial origin. I am not certain why some interstitial pneumonias improve slowly—possibly because of persistent bronchial occlusion.

I believe that exploratory operation should have been carried out because a primary bronchogenic carcinoma cannot be excluded; however, for the benefit of this exercise, I shall favor an inflammatory lesion, either an unresolved interstitial pneumonia or tuberculosis.

DR. BENJAMIN CASTLEMAN: Dr. Sprague, you were the first physician to see this patient; would you say a word?

DR. HOWARD B. SPRAGUE: This very apprehensive man had had a myocardial infarction ten years previously and had been carefully followed by his physician. When he moved to Boston last year he was referred to me for a checkup. When I saw him six weeks before admission I noted this suspicious shadow, —my only claim to fame in the field of radiology,— but I was not sufficiently sure of what I saw to regard it as benign. I asked first if earlier x-ray films were available. The x-ray films taken ten years previously were located and did not demonstrate anything abnormal. (By the way, this reveals the value of retaining x-ray films for a considerable time before they are thrown away.) I sent the patient to Dr. Richard Schatzki, and his films were interpreted as showing a definite shadow in this area that was, he thought, suspicious of bronchogenic carcinoma, but he said that the bronchoscopic examination would probably be negative. I then referred the patient to Dr. Sweet for further studies.

DR. HANELIN: The films taken ten years before admission show an essentially normal chest. There is a somewhat atypical arrangement of vessels at the left hilus, but it is obvious that whatever has taken place occurred since then.

DR. EDWARD B. BENEDICT: I do not think one can always predict when a bronchoscopic examination will be negative. We would not do them if we knew they were going to be negative. As a matter of fact this one was negative, but that does not rule out carcinoma beyond the reach of the bronchoscope, as Dr. Hanelin pointed out.

DR. RICHARD H. SWEET: The only reason I suggested a bronchoscopic examination was that I thought Dr. Benedict might obtain washings from the bronchus. I did not think he would see this lesion because the patient had never had any symptoms and had not raised sputum. I believe very firmly, as I think most physicians do, that these single shadows discovered in the lung fields should be regarded with as much suspicion as a single nodule in the breast or thyroid gland and should be explored. Often, when they are found incidentally like this in a phase when no symptoms are present, we have the best chance that we shall ever have of curing carcinoma of the lung. When the carcinoma is in the major bronchus the cure rate is very low.

I was impressed by Dr. Sprague's finding the shadow, and I think he is to be commended for it. It shows, though, that there are exceptions to the statement that used to be made by Dr. George Holmes, once the head of the Department of Radiology, that no cardiologist should be allowed to have a fluoroscope because he only watched the heart beat and never saw anything else.

At operation this lesion had the gross characteristics of carcinoma, so far as we surgeons could tell. Frequently, we cannot distinguish from feeling and looking at a nodule in the lung whether it is carcinoma or an inflammatory lesion any more than we can in the sigmoid, cecum, sometimes the stomach or other parts of the body. The lesion felt heavy, which is one of the characteristics of carcinoma of the lung. The only clue that this was not a carcinoma was that it was adherent to the pleura and that the adhesions were very vascular, indicating two things: that it probably was inflammatory and that it had been there quite a long time—although not for many months because then the adhesions would not have been so

vascular. I believed that the best way to handle this was to do a lobectomy.

Clinical Diagnosis

?Carcinoma of left-lower-lobe bronchus.

Dr. Joseph Hanelin's Diagnosis

Inflammatory lesion of lung, ?unresolved interstitial pneumonia.

Anatomical Diagnosis

Lipoid pneumonia.

Pathological Discussion

Dr. Castleman: I was called to the operating room before Dr. Sweet did the lobectomy. He cut a piece out of the lesion for a frozen-section diagnosis because if it proved to be carcinoma he might have considered doing a pneumonectomy.

Dr. Sweet: Yes; I should have said that. We handled this in the same way that we handle a breast tumor; we did a biopsy and called Dr. Castleman to look at it. If it had been a carcinoma I might have decided, but not necessarily, to do a pneumonectomy.

Dr. Castleman: Before Dr. Sweet cut into this lesion I noticed that the surface was deeply puckered —an appearance seen with carcinoma and often with healed inflammatory lesions, especially lipoid pneumonia. As Dr. Sweet cut into it, I thought I could see something oozing out that looked fatty. A frozen section on the biopsy confirmed the fatty nature of the tissue—a classic lipoid pneumonia. A lobectomy was performed. The fixed microscopical sections of the lesion showed the empty spaces, where fat had fallen out during the preparation, around some of which were foreign-body giant cells and fibrosis—the characteristic picture of lipoid pneumonia.

Dr. Hanelin: It is not supposed to occur in that location.

Dr. Castleman: According to Brock,[2] who has made a very careful study of the anatomy of the bronchial tree, material that is aspirated by a person lying on his back will be most likely to enter the superior segment of the lower lobe since this is the most dependent bronchus. This is, for example, a common site for lung abscesses.

Dr. Hanelin: Was there a history of ingestion of mineral oil?

Dr. Sweet: After the operation I talked to the patient's wife and told her it might be a lipoid pneumonia from aspiration of an oily substance. "Oh," she said, "he has been a chronic user of nose drops all his life." I must confess that I had not given it the slightest thought before the operation; I have never seen a lipoid pneumonia due to aspiration of oily nose drops in the superior segment of either the upper or the lower lobe.

Dr. Castleman: Since most people take nose drops in the supine position and usually at night before going to bed, the superior segment of the lower lobe should get most of the aspirate. Also, Dr. Aubrey O. Hampton,[3] of Washington, D. C., formerly radiologist-in-chief here, who recently studied a large series of these lesions detected in survey chest films and proved by resection, reports that they can be found anywhere in the lung. The superior segment of the lower lobe is not an uncommon site.

Dr. Sprague: The interesting thing about this is that the patient was given oily nose drops about twenty-four years before admission by another physician and had kept refilling the prescription ever since. The physician who referred him to me had no knowledge of that. The patient believed that something was chronically wrong with his sinuses and was always putting in the nose drops. What particular circumstances made this pneumonia appear at this time I do not know. All of us were trapped in this hidden pool of oil—like a group of dinosaurs.

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CASE 40222

Presentation of Case

A twenty-six-year-old laborer was admitted to the hospital because of abdominal pain.

Two weeks previously, after a severe emotional upset, he went on a bout of drinking that lasted two days. Seven days before admission "indigestion" and an upset stomach developed, with queasiness but no pain. The next day, shortly after a turkey dinner, he began to have steady epigastric pain, which was sharp and increased markedly in severity, with radiation to the back but not to the shoulders. It was not improved with food, milk or doubling up but subsided completely with sleep, only to recur half an hour after rising in the morning, continuing with progressive severity throughout the day. Five days before entry the urine became dark, and the stools light. The appetite decreased but later improved two days before admission. He believed that he was pale but did not note jaundice. Three days before admission he had severe nausea with vomiting but without blood or coffee-grounds material, and since then he had felt very weak. At that time his physician told him that he had an ulcer, and treated him with phenobarbital and rest. He had continued to smoke a package of cigarettes daily throughout his illness. He denied having been in contact with anyone who had jaundice.

He had not had any recent transfusions but may have had some injections once three months before admission when he was admitted to another hospital unconscious and had a scalp laceration sutured, after having been in a fight.

He denied serious infectious diseases in the past or previous jaundice. A year before admission he had an episode of epigastric pain diagnosed by his physician as due to a peptic ulcer. This diagnosis had not been confirmed, however, and the patient had not had any other gastrointestinal symptoms. He admitted to considerable alcoholic intake, with frequent drinking sprees.

Physical examination showed a jaundiced man in no real distress. There were discrete, nontender palpable lymph nodes in the cervical, supraclavicular, axillary and inguinal regions. The head and neck were otherwise normal, as were the heart and lungs. The abdomen was soft, without spasm. There was an area of tenderness to light palpation in the right epigastrium. The liver edge was felt 1 or 2 fingerbreadths below the right costal margin but was not tender. The spleen was not palpably enlarged, and there were no other abnormal masses.

The temperature was 98.6°F., the pulse 72, and the respirations 20. The blood pressure was 130 systolic, 80 diastolic.

The urine had a specific gravity of 1.025 and was otherwise normal except for bile. The urinary urobilinogen was 1.1 Ehrlich units. Examination of the blood revealed a hemoglobin of 13.5 gm. per 100 cc. and a white-cell count of 3400, with 48 per cent neutrophils, 42 per cent lymphocytes, 6 per cent atypical lymphocytes, 2 per cent eosinophils and 2 per cent basophils. The serum total protein was 6.6 gm., the albumin 3.9 gm., the globulin 2.7 gm., the amylase 27 units, the total bilirubin 7.7 mg., and the alkaline phosphatase 12.0 units per 100 cc. The prothrombin time was 13 seconds (normal, 13 seconds). The thymol turbidity was 2.0 units per 100 cc. with a negative flocculation, and the cephalin flocculation + in twenty-four and forty-eight hours. The heterophil-antibody test was negative. A stool specimen was light yellow and guaiac negative. A plain film of the abdomen and a gastrointestinal series did not give any abnormal findings.

During the first week in the hospital the patient seemed somewhat more ill with mild anorexia, weakness and malaise but was still afebrile. The note was made that he seemed surprisingly well in view of the deep jaundice. At this time he had marked punch tenderness over the liver area, but the liver edge was no longer palpable. During this period the serum bilirubin rose to 9.5 mg., and the alkaline phosphatase to 19.1 units per 100 cc. The cephalin flocculation was ++ in twenty-four and +++ in forty-eight hours; a second thymol-turbidity determination was 3.0 units per 100 cc., with a negative flocculation. Urinalysis remained unchanged; a second white-cell count was 6500, with 74 per cent neutrophils, 21 per cent lymphocytes, 3 per cent atypical lymphocytes and 2 per cent eosinophils.

During the following week the patient remained about the same clinically. The urinary urobilinogen was 3.8 units per 100 cc. The serum total bilirubin was 16.0 mg., the alkaline phosphatase 28.6 units, the thymol turbidity 3.0 units, the cholesterol 359 mg., and cholesterol esters 117 mg. per 100 cc. The prothrombin time was 15 seconds (normal, 13 seconds). The white-cell count was 10,200; the sedimentation rate was 1.4 mm. per minute. On the twenty-third hospital day the alkaline phosphatase was 29.2 units, and the serum total bilirubin 19.0 mg. per 100 cc. On the twenty-seventh hospital day jaundice seemed lighter, but there was still tenderness over the liver area. Physical examination was otherwise unchanged. The serum bilirubin was 13.6 mg., and the alkaline phosphatase 44 units per 100 cc. The cephalin flocculation was ++ in forty-eight hours, the prothrombin time 13 seconds (normal, 13 seconds), the thymol turbidity 3.0 units per 100 cc., and the thymol flocculation negative. On duodenal drainage 50 cc. of golden-yellow fluid was recovered; this contained a rare white cell and many irregular yellowish crystals. Subsequently, the serum bilirubin fell to 8.2 mg. per 100 cc., but the alkaline phosphatase remained at a level of 26.9 mg. per 100 cc. A roentgenogram of the chest and a metastatic x-ray series were normal. Throughout the entire hospital stay the temperature and pulse continued to be normal. Stool specimens were frequently examined; all ranged from light tan to clay colored, and only two were guaiac positive (1 was ++), having been collected on the sixteenth and twenty-third hospital days. The clinical picture was usually characterized by a good appetite and a sense of feeling fairly well although on occasional days the patient complained of anorexia and malaise. On the thirty-seventh hospital day an operation was performed.

Differential Diagnosis

Dr. John B. Stanbury*: I should like to see the plain film of the abdomen and any of the other films that may be pertinent. I am particularly interested in the size of the liver and the spleen.

Dr. C. C. Wang: The spleen does not appear enlarged. The tip of the liver lies approximately 3 cm. above the iliac crest; I do not know how large the liver is. No gallstones can be seen in the right upper quadrant of the abdomen. The examination of the chest is essentially negative. The gastrointestinal series gives no definite evidence of esophageal varices; the esophagus and the stomach appear normal. There is an extrinsic pressure defect on the apex of the duodenal cap, which is occasionally seen with an enlarged gall bladder. The duodenal loop is not widened and shows no extrinsic or intrinsic defect.

*Assistant physician, Massachusetts General Hospital.

DR. STANBURY: Can you be sure about the gall bladder?

DR. WANG: I am not too sure about that.

DR. STANBURY: This is obviously a case for the differential diagnosis of jaundice. First of all we can dismiss prehepatic jaundice. There was no evidence of a hemolytic process. There was ample bile and no suggestion of hemoglobin in the urine, and the patient was not anemic.

There are three general groups of hepatobiliary disease that I should like to discuss, because in one or more of these resides the diagnosis that fits this case. The first is cirrhosis of the type often seen in alcoholism or in patients who have been ill from such toxic agents as carbon tetrachloride and who have had severe nutritional deficiencies. There is ample reason to suspect that this patient was an incipient alcoholic. Why liver disease develops in alcoholics is certainly not clear. I do not know whether it is a simple nutritional problem, whether the imbalance of the metabolic mixture results in liver disease in a fashion similar to that in a patient with severe protein depletion, whether it is due to an avitaminosis secondary to a poor diet or whether the liver is affected by some toxin, either the alcohol itself or some contamination of the alcohol. In this particular case it is very difficult to make a diagnosis of early Laënnec cirrhosis in a phase of acute hepatic insufficiency. These patients have large livers, spider hemangiomas and other evidence of Laënnec's cirrhosis. Also, there was no suggestion of exposure to any toxicant, such as carbon tetrachloride or *Amanita phalloides*, to account for liver disease. It is possible, of course, that alcoholism contributed to the liver damage, but I do not think I could accept a diagnosis of fatty infiltration of the liver accompanying incipient portal cirrhosis as a cause of the symptoms that this patient presented.

The second group of diseases to be considered comprises the viral infections: viral hepatitis of the infectious variety or of the variety that is spread by transfusions or needles—that is, homologous serum jaundice. A number of features in this case are consistent with viral hepatitis. A protracted course and continued jaundice are often seen with the ordinary form. The nausea at first, the occasional bouts of fatigue and malaise and the abnormal leukocytes reported on two occasions are suggestive of infectious hepatitis. Certain features in the case, however, are against this diagnosis, the principal ones being the liver-function tests. The outstanding of these is the alkaline phosphatase, which began at a low figure and rose rapidly to 44 Bodansky units per 100 cc. as the disease progressed. This is not consistent with the ordinary case of viral hepatitis, in which the alkaline phosphatase is rarely higher than 12 units per 100 cc. Watson and Hoffbauer[1] have described what they consider to be a chronic form of viral hepatitis that seems to attack the biliary system. Those patients present many of the features of obstructive jaundice in that they have a high alkaline phosphatase and often no laboratory evidence of parenchymal damage. Histologically, the cellular structure of the liver may appear relatively normal, without evidence of the necrosis seen in infectious hepatitis, but there is cholangitis, with bile stasis, cholangiole proliferation and plugging of the finer biliary radicles with inspissated bile. One could make a good case for this type of disease in this patient, whose illness may have begun with viral hepatitis or perhaps homologous serum jaundice and later developed into the picture described by Watson and Hoffbauer.[1] This is a rare condition, however, and its very existence has been challenged by a number of observers.

The third type of hepatobiliary disease is that which arises because of extrahepatic obstruction. This may be cholelithiasis, with a stone passing down the common duct leading to obstruction, or pressure on the common duct by nodules of scar tissue or a malignant lesion of the head of the pancreas or the ampulla. It is quite impossible to make a diagnosis of carcinoma of the ampulla in a patient twenty-six years of age, for this is a disease of middle or older years.

The patient had lymphadenopathy. It is conceivable that enlarged lymph nodes obstructed the common duct and led to jaundice. Nothing in the past history was suggestive of Hodgkin's disease or of a related disease in which there are enlarged lymph nodes. With lack of other evidence lymphoma can be dismissed as a possibility.

We are left with scarring of the common or hepatic duct or cholelithiasis with stone in the duct. A good case can be made for cholecystitis, cholelithiasis and stone in the common duct. Although one would like to see a higher white-cell count, fever and more typical radiation of the pain, the findings in general are not at all inconsistent with the diagnosis. In addition there were yellowish crystals, presumably calcium bilirubinate, in the duodenal drainage. Calcium bilirubinate crystals in the biliary drainage are abnormal and are found in cholecystitis. I shall therefore have to be content, in spite of this patient's youth, with a diagnosis of cholelithiasis and cholecystitis and a stone in the common duct.

Three operations were possible: a lymph-node biopsy, a punch biopsy of the liver and an exploration of the right upper quadrant. I suspect that a needle biopsy was done, and that bile stasis and proliferation of cholangioles were found; perhaps afterward, at exploration, a stone was found in the common duct.

DR. WARREN POINT: Dr. Stanbury's discussion has been very clear; the diagnosis was not quite so clear in the hospital, however, and several of the consultants thought it was the type of cholangiolitis that Watson and Hoffbauer[1] described. On several occasions a biopsy was planned, but since the jaundice became lighter the biopsies were canceled. Finally one was done.

Clinical Diagnosis

Cholangiolitic hepatitis.

Dr. John B. Stanbury's Diagnosis

Cholecystitis and cholelithiasis, with obstruction of common duct.

Anatomical Diagnosis

Cholecystitis and cholelithiasis with obstruction of ampulla of Vater.

Pathological Discussion

Dr. Benjamin Castleman: As Dr. Stanbury suggested, Dr. Point did do a needle biopsy of the liver. The bile canaliculi were plugged with bile—the classic appearance of bile stasis. With this as evidence the surgeons found, as Dr. Stanbury predicted, a gall bladder full of stones, with one impacted in the ampulla of Vater; the gall bladder was removed and the patient was discharged, we hope cured.

Dr. Point: He did have one complication: he became quite schizophrenic after the operation; there was some indication that his personality had been somewhat similarly affected in recent years. He recovered from the acute complication and went home apparently cured.

Several things should be pointed out in this case. The continued absence of the bile in the stools is good evidence that there was no chronic hepatitis of any kind, and, secondly, the alkaline phosphatase of 44 units per 100 cc. is good evidence for mechanical obstruction but not absolute proof. We have seen patients with cirrhosis of the liver and an alkaline phosphatase of 35 Bodansky units per 100 cc.; it can be high at times.

Dr. Castleman: Should you like to comment on the incidence of stones at the age of twenty-six?

Dr. Point: We do not often see patients of that age with gallstones; the incidence is very low.

Dr. Castleman: Lichtman[2] reports that less than 1 per cent of the patients with gallstones are under twenty years of age.

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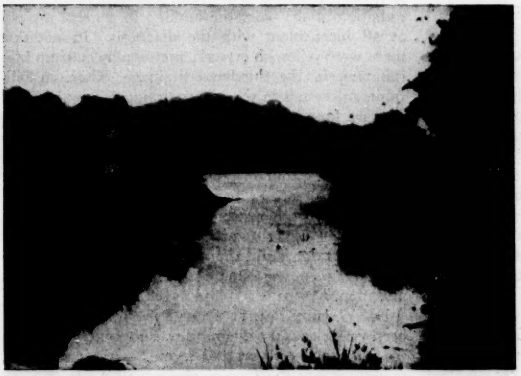

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27. Still Waters

Exhibited at Annual Meeting Massachusetts Medical Society, 1953

Oil Painting by
Elizabeth Z. Kleinman

Assistant, Department of General Practice, New England Hospital

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COMMENCEMENT

THE *Journal* takes the occasion, in this month of roses and of brides, to recognize also one of the facts of academic and cultural life — namely, that in the late spring comes the termination of formal study commonly called commencement. Unlike birth, as Wordsworth defined it, this commencement is supposed not to be a sleep and a forgetting.

Two appropriate contributions published elsewhere in these pages constitute the *Journal's* part in this recognition. They are its prize-winning student essay, submitted by Mr. Donald I. Matern, who has recently emerged, or is about to emerge, from the cloistered halls of Cornell University Medical College, and the annual Shattuck Lecture of the Massachusetts Medical Society, delivered last month by Dr. James M. Faulkner, dean of Boston University School of Medicine, on "Medical Education and the Physician."

The *Journal* takes special pride in its interest in these matters of commencements and the educational process that precedes them because it believes itself to be especially favored by the medical students of the country, nearly 5500 of whom are among its subscribers. It avers that the regard is mutual.

Mr. Matern's essay, following the ground rules prescribed for the course, consists of the report and discussion of a case that he has studied as part of his academic duties. Concerned with the drama of "Hypokalemia Accompanying Hyperchloremic Acidosis after Ureterosigmoidoscopy," it has been presented with intelligence and integrity. Causing the judges many a wakeful night in their determination to put first things first, if possible, was the second-prize winning paper, on "Postoperative Hypoparathyroidism," by Donald J. Lauber, of the University of California Medical School. All the papers submitted, in fact, reflected the high quality of teaching in the medical schools today, as well as providing evidence that the caliber of the country's medical graduates has as yet demonstrated no deterioration.

Dr. Faulkner has taken the opportunity of depicting the development of medical education in Massachusetts and the part played in it by the Massachusetts Medical Society, which was a determining factor for many years in the maintenance of standards in education as well as in practice. It was not, in fact, until 1922 that the Council of the Society gave up its own approval of medical schools, although the American Medical Association had assumed the same duty in 1845. That the maintenance of some sort of standards was necessary is attested by the rank growth of such schools in the second half of the nineteenth century, their number reaching 160 in the United States at one time.

There are difficulties enough associated with medical education, which may be considered the most complicated of the educational processes; its major problems are threefold. The first of these is the keeping up to date of medical teaching, for in no branch of practical learning is knowledge making more rapid progress. In this modernization the important change is the shift in emphasis from human diseases to man himself in relation to his environment—the bionomics of the human subject. With reverence for the original man to whom the words were applied, Pilate's *Ecce homo* has taken on a significance that includes all mankind.

The second in the trilogy of problems with which medical educators are unceasingly engaged is the unprecedented cost of the commodity they have to purvey; the third is the selection of the material to be educated and the assurance, so far as possible, of its quality. Despite the demands from various quarters for a greater number of practicing physicians there is today, as has been indicated even in these pages, a relative shortage of young men and women of sufficiently high caliber who wish to study medicine. And this student material is the cornerstone on which the constantly renewed structure of medical practice and medical progress must inevitably rest.

The difficult matter of selecting the human material to be medically educated and if possible of establishing the type most adapted to the practice of medicine occupied a position of prominence at the First World Conference on Medical Education held in London last summer. It was decided then that an important prerequisite for the ideal medical student is a liberal college education. In regard to his personal qualifications it was found, as some may remember, that efforts at identifying him resulted in a fusion of images bearing an engaging resemblance to a Greek god.

ANNUAL MEETING IN RETROSPECT

THE meeting of the Council preceding the hundred and seventy-third annual meeting of the Massachusetts Medical Society took place on Monday evening, May 17, at the Hotel Statler, 278 councilors being present. Under the skilled and patient guidance of President Hagler and Secretary Buck this meeting was one of the most smoothly run in recent years, although the volume of controversial business that came under discussion and the number of discussers that required to be heard made it also a protracted one.

Alert as always in protecting the principles of private practice, the Committee on State Legislation had presented a supplementary report relative to the act permitting Blue Cross to contract "with any agency of the United States of America, of the Commonwealth or any city or town within the Commonwealth for the purpose of providing hospital service or reimbursement for other health services."

The burning question in discussion revolved around the definition of "other services." These, as the Council was picturesquely assured by proponents of the law, applied to such nondoctor services as the purchase of bedpans and wheelchairs. Other councilors, viewing the extension of powers with greater alarm, saw in it the possibility of an implementation that might lead to a system of socialized medicine under joint Blue Cross and governmental jurisdiction. After considerable ventilation of the subject the Council voted to uphold the recommendations of the Executive Committee that it be referred back to the Committee on State Legislation. The consensus was that rephrasing and clarification of the act by the next legislature was needed so that no shadow of a doubt regarding the exploitation of physicians' services can remain.

The Committee on Hospital and Professional Relations made certain recommendations clarifying matters relating to hospital staff appointments and revocation of staff privileges, according to the mechanism established by the Joint Commission on Accreditation of Hospitals. These recommendations were accepted with minor amendments made by the Executive Committee.

A discussion of the report of the Committee on By-Laws and Council Rules revealed strong support of a proposed change in the Medical Defense Act of the Society relative to the part that fellows must occasionally play in the commitment of persons to a mental institution; fellows are sometimes in need of greater legal protection than has hitherto been available.

The recommendations of the Committee on Redistricting that Martha's Vineyard be transferred from Bristol South to Barnstable and that a new district be created from adjacent parts of Middlesex South and Norfolk were adopted. The latter gave rise to considerable discussion and a degree of opposition, largely from members of the two districts involved who lived outside the area that would comprise the contemplated new district.

The report of the Committee on Welfare Problems elicited an anticipated discussion. Much of the widespread dissatisfaction with the present policies of the Department of Public Welfare of the Commonwealth appears to have resulted from the arbitrary and uncompromising attitude of the present commissioner. The report was referred back to the Committee for further attempts at arbitration.

During the course of the evening the newly elected officers whose nominations were published in the *Journal* on April 29 were presented to the Council, and at the close of the session President Tripp announced his committee appointments for the coming year.

The remainder of the one hundred and seventy-third annual meeting of the Massachusetts Medical Society went off according to the announced and publicized program. At the official annual meeting within the general annual meeting, on the day following the annual meeting of the Council (some new terminology might be considered), the annual oration was delivered by Dr. Basil E. Barton, the President delivered his message on the state of the Society, amendments to the *By-Laws* were accepted, 26 veterans of fifty years of active membership received their commemorative lapel buttons, and the most promising fourth-year student from each of the three medical schools in the state received his prize. The recipients were Mr. Joseph Van Der Meulen, of Boston University School of Medicine, Mr. Walter Emery Klingensmith, of Harvard Medical School, and Mr. Edwin Ray Guise, Jr., of Tufts College Medical School. The prizes consisted of first editions of Cushing's life of Osler, handsomely rebound.

On the following morning, May 19, the Shattuck Lecture was delivered by Dr. James M. Faulkner, dean of Boston University School of Medicine, and at the annual dinner Dr. Charles S. Houston, of Exeter, New Hampshire, told of his experiences last summer in leading an assault on K2, the second highest peak of the Himalayas. It is regretted that illness prevented the attendance of Dr. Edward J. McCormick, president of the American Medical Association, who also had accepted an invitation to address the dinner meeting.

NATIONWIDE ALERT

On Monday, June 14, and Tuesday, June 15, the first nationwide Civil Defense Training Exercise will be held for twenty-four hours, as requested by the President two months ago. The alert will actually be more than continental in scope, for it will be participated in by the United States, Canada, Alaska, Puerto Rico and the Hawaiian Islands. The exercise will consist of two parts, one for public participation, limited to June 14, and a separate training problem for federal and state control centers that will cover the entire twenty-four-hour period.

The exercise in which the public must participate will start with a yellow alert announced only by radio broadcast at 9:30 a.m. on June 14; the red alert announced by audible sirens will begin at 10:00 a.m. and will be the signal for all traffic to stop and for all persons to take shelter. It will come to an end when the audible white alert is sounded at 10:10 a.m. At 10:55 a.m. a yellow alert will draw back the curtain for dress rehearsal of key personnel who will man state, regional, sector and local control centers. In Region I, which includes New England, New York and New Jersey, atomic attacks on Boston, Providence, Hartford, Schenectady, Buffalo, Newark and New York will be simulated and will be appropriately met—on paper—since all movement of apparatus and personnel other than that required to man the centers will also be simulated. At successive hours, as the sun moves westward, other time zones will be alerted and will experience their catastrophes until 42 simulated bombs will have dropped, from sea to shining sea.

Such a practice alert is a matter to be taken seriously by the entire nation, doing all that can be done at the present to prepare for an eventuality that is within the range of possibility. As with the mice who voted to bell the cat there are weaknesses in the potential chain of events that have not as yet been overcome. The first, obviously, is the present impossibility of preventing the dropping of the bomb. The second is the failure to come to a clear understanding of what to do once it is known that the bomb will be dropped, for no clear decision has yet been announced between taking shelter and attempting a mass evacuation of a large city in the few brief hours that may be available.

A population in a panic is a population out of control, and countless thousands will jam the highways under any circumstances. A controlled evacuation is something to talk about only; no emergency evacuation could be controlled in the face of threatened mass annihilation.

VICISSITUDES OF REINSURANCE

Government reinsurance of voluntary health prepayment plans has had its share of heavy going since it was first proposed by the present Administration in the President's health message to Congress on January 18. Opposed, although temperately, by the American Medical Association on the grounds that voluntary health insurance is doing well enough without governmental intervention and that so much regulatory power should not be vested in the Secretary of Health, Education and Welfare, it is rejected also by Physicians Forum, Incorporated, on somewhat different grounds. Physicians Forum criticizes it because it is not compulsory national health insurance and because it extends eligibility to insurance companies as well as to nonprofit organizations.

The Annual Conference of Blue Cross and Blue Shield Plans, meeting early in April, was given a briefing and reassurances on reinsurance by youthful Roswell B. Perkins, assistant secretary of the Department of Health, Education and Welfare. Mr. Perkins emphasized that absolutely no interference with the voluntary health movement is intended; that reinsurance is voluntary for each carrier; that the regulation of the carriers remains with the states; that it operates only where comparable reinsurance is not available; that it reinsures abnormal losses only; that the carrier coinsures, by sharing in the losses; and that the federal liability is limited to the $25,000,000 authorized, plus the reinsurance dividends.

Before the conference closed, Blue Cross, by unanimous vote of the 83 participating plans, gave its support, recognizing "the sincere intent of President Eisenhower's Administration to make comprehensive health coverage available to more people by 'encouraging and stimulating the expansion of voluntary health programs.' " The 78 Blue Shield plans, equally well mannered, patted the Administration on the back with a cautious vote to "recognize and appreciate the sincere intent of President Eisenhower's Administration to make health coverage available to more people." They expressed doubt, however, that they would ever need to invoke the bill if it were passed.

Chances for passage have generally been conceded to be slim and growing slimmer as the weeks have gone by. Not long ago, however, hopes of salvaging reinsurance were raised. HR 7700, a bill promoting construction of group-practice clinics and hospitals through government-insured loans, has received the support of Henry J. Kaiser and the American Federation of Labor, although opposed by the American Medical Association.

A strategy apparently developing at the time of this writing is that the building-loan-insurance bill, combined into a single measure with a diluted reinsurance plan, will stand a better chance of favorable action than either bill by itself. Loan insurance, it is said, has the voice of the turtle in election year.

An ingenious mechanic of Vermont has invented a very curious and useful machine for the management of fractured limbs, which will soon be presented to the profession.

Boston M. & S. J., *June 7, 1854*

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

GAY — Clarence B. Gay, M.D., of Fitchburg and Vineyard Haven, died on April 30. He was in his eighty-second year.

Dr. Gay received his degree from the University of Pennsylvania School of Medicine in 1899. He was formerly supervising censor, executive councilor and president of the Worcester North District Medical Society.

He is survived by his widow and a daughter.

HARRIS — Paul L. Harris, M.D., of Lowell, died on April 25. He was in his fifty-ninth year.

Dr. Harris received his degree from Tufts College Medical School in 1921.

McADAMS — James C. McAdams, M.D., of Fall River, died on May 9. He was in his fifty-fifth year.

Dr. McAdams received his degree from the University of Pennsylvania School of Medicine in 1926. He was a fellow of the American Medical Association and the American College of Physicians, vice-president of the New England Heart Association, a member of the American Heart Association and of the staff of the Truesdale Hospital, and formerly president of the Fall River Medical Society.

He is survived by his widow, two daughters, a son and a brother.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR APRIL, 1954

RÉSUMÉ

Disease	April 1954	April 1953	Seven-Year Median
Chancroid	2	8	3
Chicken pox	1656	3528	1973
Diphtheria	1	8	17
Dog bite	1451	1158	1160
Dysentery, bacillary	15	38	7
Encephalitis, infectious	4	1	2
German measles	439	1195	266
Gonorrhea	162	187	187
Granuloma inguinale	0	0	0
Hepatitis, infectious	117	192	11†
Lymphogranuloma venereum	0	0	0
Malaria	0	0	1
Measles	1590	413	2022
Meningitis, meningococcal	13	6	6
Meningitis, Pfeiffer bacillus	7	3	3
Meningitis, pneumococcal	5	3	2
Meningitis, staphylococcal	0	0	0
Meningitis, streptococcal	0	1	1
Meningitis, undetermined	7	11	3
Mumps	2515	1504	1346
Poliomyelitis	0	0	0
Salmonellosis	32	23	7
Scarlet fever	600*	543	578
Syphilis	180	98	136
Trichinosis	1	1	3
Tuberculosis, pulmonary	206	175	229
Tuberculosis, other forms	9	12	16
Typhoid fever	2	4	3
Undulant fever	4	1	2
Whooping cough	206	103	183

*Includes streptococcal sore throat.
†Five-year median.

COMMENT

Diseases below the seven-year median were chicken pox, diphtheria, measles and tuberculosis.

Only 1 case of diphtheria was reported during the month of April. This brings the total for the four-month period since January 1 to 9, which is identical with the figure for the same period last year. Within the past few years, remarkably low figures for this disease have become commonplace. Some years ago — in 1924, for example — the same four-month period registered 3209 cases of this disease.

Diseases above the seven-year median were bacillary dysentery, German measles, infectious hepatitis, mumps, salmonellosis, scarlet fever and whooping cough.

Although the enteric diseases — namely, bacillary dysentery, infectious hepatitis, and salmonellosis — all remained above the seven-year median for the first time in recent months, all three simultaneously showed a decrease from the preceding month.

With but one exception (1948) the incidence of 2515 cases of mumps was the highest for the month of April in the history of this state.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

The following diseases were reported from the communities named:

Diphtheria: Everett, 1.

Dysentery, amebic: Wrentham, 8.

Dysentery, bacillary: Montague, 1; Newton, 1; Worcester, 3; Wrentham, 10; total, 15.

Encephalitis, infectious: Holyoke, 1; Lexington, 1; Melrose, 1; Shrewsbury, 1; total, 4.

Hepatitis, infectious: Belchertown, 1; Boston, 12; Brockton, 11; Cambridge, 15; Carver, 1; Charlton, 1; Chelsea Naval Hospital, 5; Chicopee, 1; Everett, 1; Fall River, 4; Fort Devens, 2; Greenfield, 2; Lowell, 2; Lynn, 10; Marblehead, 1; Montague, 1; New Bedford, 1; Newton, 1; Oxford, 1; Pepperell, 1; Pittsfield, 1; Plymouth, 9; Quincy, 7; Shrewsbury, 2; Somerset, 1; Springfield, 6; Swampscott, 2; Waltham, 1; Webster, 5; Wellesley, 1; Williamstown, 3; Worcester, 5; total, 117.

Lymphocytic choriomeningitis: Beverly, 1; Norton, 1; total, 2.

Meningitis, meningococcal: Ayer, 1; Beverly, 1; Boston, 4; Cambridge, 1; Fall River, 1; Holliston, 1; Lowell, 1; Newton, 1; Stoughton, 1; Worcester, 1; total, 13.

Meningitis, Pfeiffer bacillus: Arlington, 1; Attleboro, 1; Boston, 1; Haverhill, 1; Lynn, 1; North Adams, 1; Taunton, 1; total, 7.

Meningitis, pneumococcal: Lowell, 1; Pittsfield, 1; Somerset, 1; Upton, 1; Worcester, 1; total, 5.

Meningitis, mumps: Braintree, 1; Middleboro, 1; Natick, 1; Wayland, 1; total, 4.

Meningitis, undetermined: Cohasset, 1; Dedham, 1; Fall River, 2; Falmouth, 1; Salem, 1; Southbridge, 1; total, 7.

Psittacosis: Attleboro, 1.

Salmonellosis: Arlington, 2; Beverly, 1; Boston, 4; Clinton, 1; Hingham, 1; Mattapoisett, 1; Medford, 9; Middleton, 1; Milton, 1; Newton, 1; Salem, 1; Wellesley, 1; Webster, 3; Winchester, 1; Woburn, 3; Worcester, 1; total, 32.

Trichinosis: Cambridge, 1.

Typhoid fever: Boston, 1; Fall River, 1; total, 2.

Undulant fever: Framingham, 2; Lynn, 1; Templeton, 1; total, 4.

CORRESPONDENCE

READING THE BLOOD PRESSURE

To the Editor: Many of us must have observed a difference in the blood-pressure readings of certain persons between the auditory method with the use of the stethoscope and the visual method marked by fluctuations of the needle or the mercury. The amount of variation increases with the size and the firmness of the arms of any particular subject: the larger the circumference and the consistence, the greater the diversity. The fluctuations of the needle or mercury may appear at a level as much as 8 mm. above that at which any sound is heard and continue as much as 10 mm. after the last audible sound.

Answers to the following questions seem to be essential:

How much of a factor is the acuteness of one's hearing?

Is there a significant factor in the relation between the width of the inflatable part of the arm band and either the size or the consistence of the arm of the subject?

What are the respective values of the two methods so far as relative reliability and absolute correctness are concerned?

G. W. HAIGH, M.D.

Worcester, Massachusetts

RESTORATION OF LICENSE

To the Editor: At a meeting of the Board of Registration in Medicine held April 29, 1954, it was voted to restore the registration to practice medicine of Dr. Leo J. Mandeville, 5 Taylor Street, Holyoke, with the recommendation that his narcotic license be withheld.

ROBERT C. COCHRANE, M.D., *Secretary*

State House
Boston

REVOCATION OF LICENSE

To the Editor: At a meeting of the Board of Registration in Medicine held April 29, 1954, it was voted to revoke the registration to practice medicine of Dr. William E. Cohen, 67 Beech Street, Roxbury.

ROBERT C. COCHRANE, M.D., *Secretary*

State House
Boston

BOOK REVIEWS

Textbook of Gynecology. By John I. Brewer, M.D., Ph.D. 8°, cloth, 532 pp., with 146 illustrations. Baltimore: Williams and Wilkins, 1953. $10.00.

This standard text in gynecology presents the materials of its subject under the appropriate pathological captions in two parts, each containing a dozen chapters. The first part, which is newly written for this publication, pursues the teaching method dealing with discussion and elaboration of individual entities of disease and descriptions of the lesions that they produce. The second, which is based on an earlier book by Dr. Brewer (*Gynecology*) published in 1950 by Thomas Nelson and Company, adopts rather the didactic method of clinical symptomatology, approaching the subject from the standpoint of the patient's complaints and proceeding to the diagnosis and treatment of the condition producing the trouble. This is the method that for several recent years has been exclusively employed, with distinct advantage, in the teaching of gynecology at Northwestern University Medical School, where the author is currently professor of gynecology and obstetrics. The entire work reflects not only his views but also those of his predecessor and teacher, Dr. Harold O. Jones, to whom the book is dedicated. It is abundantly illustrated with 146 photographs and photomicrographs, and has an excellent index.

ROBERT M. GREEN, M.D.

Extrasystoles and Allied Arrhythmias. By David Scherf, M.D., and Adolf Schott, M.D. (Heidelberg), M.R.C.S. 8°, cloth, 531 pp., with 213 illustrations. New York: Grune and Stratton, 1953. $15.50.

This reference book of great value continues the European tradition of the study of the heart from the golden era of Wenckebach, Rothberger and Winterberg. The bibliography is strongly European, which is a good thing for physicians from the United States. The chapter on historical orientation is excellent, with illustrations and original quotations in Latin as far back as Galen. Of the 11 other chapters 8 are primarily concerned with extrasystoles, and 1 each with pararrhythmias, pulsus alternans and flutter, fibrillation and paroxysmal tachycardia.

Although most of the book is of greatest interest to cardiac specialists it contains so much clinical material that it could well be in the library of any physician concerned with the care of patients with disorders of the heart beat. Treatment, as such, is confined to 8 pages, but this by no means shows the extent of the therapeutic material, since, for example, an entire chapter of 22 pages is devoted to the subject "Extrasystoles, Drugs and Electrolytes." The format and the publisher's contribution to this book are in keeping with the obvious intent that this should be a definitive and permanent addition to medical literature. In my opinion it will be.

HOWARD B. SPRAGUE, M.D.

Psychosomatic Approach to Gynecology and Obstetrics. By Fritz Wengraf, M.D. 8°, cloth, 346 pp. Springfield, Illinois: Charles C Thomas, 1953. $6.75. (Publication No. 164, *American Lecture Series.*)

This volume is a monograph in the Bannerstone Division of American Lectures in Gynecology and Obstetrics, edited by E. C. Hamblen, M.D., professor of endocrinology at Duke University School of Medicine. The author, Dr. Fritz Wengraf, adjunct neuropsychiatrist at the Beth Israel Hospital in New York City, who has had abundant experience and training in gynecology, obstetrics and psychiatry, points out in the preface that psychosomatic medicine, of which his work is an example, has both "a general and a specific connotation, and the two are, externally at least, irreconcilable": the former implies a philosophic attitude toward illness, and an interest in the patient as a whole instead of merely in his disease; and the latter emphasizes the emotional element in the etiology of certain clinical entities and the utilization of this element both in theory and in practice.

From this point the entire text attempts to apply and clarify this psychiatric approach to the field of gynecology and obstetrics. It is divided into six principal parts. The first deals with the nature, psychodynamics and differential diagnosis of functional disorders. The second discusses constipation as an example of these. The third deals with minor gynecology and the phenomena of puberty, dysmenorrhea, psychosomatic uterine bleeding, functional amenorrhea, psychogenic leukorrhea, frigidity and its sequelae, and the menopause. The author has found the psychiatric approach particularly valuable in the management of dysmenorrhea, frigidity and hyperemesis gravidarum. The fourth part considers major operative gynecology from the standpoints of preoperative care, postoperative neuroses and reactions to anesthesia. The fifth concerns the psychosomatic aspects of obstetrics under the captions of gestation, parturition, confinement, lactation and abortion. And the last summarizes the methods of psychotherapeutics applicable under all these conditions.

The book has no pictorial illustrations, but admirable indexes of authors and subjects, and a copious bibliography of 516 entries and references. It is a valuable modern contribution to one of the oldest aspects of medical science and practice.

ROBERT M. GREEN, M.D.

NONCLINICAL NOTES

SHATTUCK AWARD

Dr. Ira V. Hiscock, professor of public health, Yale University School of Medicine, has received the 1954 Shattuck Award for outstanding and meritorious contributions to the field of public health.

Dr. Hiscock was recently elected president of the Association of Schools of Public Health of the United States and Canada, and also received the 1954 Medal of the Connecticut Division of the American Cancer Society.

PROFESSOR OF TROPICAL PUBLIC HEALTH

Dr. Thomas H. Weller, a leading investigator in the field of poliomyelitis, has been appointed Richard Pearson Strong Professor of Tropical Public Health at the Harvard School of Public Health. Dr. Weller is the first holder of the first endowed professorial chair at the School.

CONNECTICUT VALLEY RADIOLOGIC SOCIETY

At a recent meeting of the Connecticut Valley Radiologic Society the following officers were elected for the coming year: president, Dr. Charles C. Verstandig, New Haven,

Connecticut; vice-president, Dr. Arthur J. Harrigan, Springfield, Massachusetts; secretary-treasurer, Dr. B. Bruce Alicandri, Springfield, Massachusetts.

NOTICES

INTER-SOCIETY CYTOLOGY COUNCIL

The second annual meeting of the Inter-Society Cytology Council will be held at the Hotel Statler, Boston, November 12 and 13. Registration will be open to anyone interested in cytology. Medical students, interns and residents will be admitted without charge. (Registration fee for physicians, $5, for technicians, $2.)

Abstracts of papers, limited to 200 words, with three copies of the title, may be sent to Dr. John B. Graham, chairman, Program Committee, 32 Fruit Street, Boston, Massachusetts, before July 15. It is suggested that emphasis be placed on the endometrium and lesions of the gastrointestinal and urinary tracts. Abstracts of all papers accepted will be published in the official program. Additional information may be obtained from the Secretary-Treasurer, Inter-Society Cytology Council, 634 North Grand Boulevard, St. Louis, Missouri.

AMERICAN INSTITUTE OF DENTAL MEDICINE

The annual meeting of the American Institute of Dental Medicine will be held at the Desert Inn, Palm Springs, California, October 31 to November 4. Applications and further information may be obtained from Miss Marion G. Lewis, Executive Secretary, 2240 Channing Way, Berkeley 4, California.

AMERICAN ASSOCIATION OF BLOOD BANKS

The seventh annual meeting of the American Association of Blood Banks will be held at the Shoreham Hotel, Washington, D.C., September 13-15.

HOSPITAL COUNCIL OF METROPOLITAN BOSTON

The annual meeting of the Hospital Council of Metropolitan Boston will be held on June 7 at the Mason Memorial Building, 14 Somerset Street, Boston. The luncheon will be served at 12:15 p.m. Dr. Chester S. Keefer will speak on the subject "Administration Health Plans." Physicians are invited. Reservations must be made before June 5, at RI 2-2000.

NEW ENGLAND PEDIATRIC SOCIETY

The next two meetings of the New England Pediatric Society will be held on Wednesday, September 22 and December 8, in the Auditorium of the Jimmy Fund Building. Refreshments and dinner will be served at the Longwood Towers, Brookline.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

Applications for the examinations for certification by the American Board of Obstetrics and Gynecology will be accepted by the secretary, Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6, Ohio, until October 1.

SOCIETY MEETINGS AND CONFERENCES

June 7. Hospital Council of Metropolitan Boston. Notice above.
June 11–13. American Electroencephalographic Society. Page 748, issue of April 29.
June 13–17. American Society of Medical Technologists. Page 444, issue of March 11.
June 14–16. American Neurological Association. Page 540, issue of March 25.
June 15–18. Medical Library Association. Page 491, issue of March 18.
June 17–19. American Geriatrics Society. Page 266, issue of February 11.
June 17–21. Pan American Congress of Ophthalmology. Page 540, issue of March 25.
June 19 and 20. Society for Investigative Dermatology. Page 540, issue of March 25.
June 23. Tufts Medical Alumni AMA Dinner. Page 585, issue of April 1.
July 22 and 23. International College of Surgeons. Regional Meeting. Page 828, issue of November 12.
July 23–29. International Cancer Congress. Page 914, issue of November 26.
July 26–31. International Congress of Gynecology and Obstetrics. Page 400, issue of March 4.
August 1–7. Pan-American Congress of Pediatrics. Page 850, issue of May 13.
August 17–20. Argentine Congress of Thoracic Surgery. Page 708, issue of April 22.
September 6–10. International Poliomyelitis Congress. Page 399, issue of March 4.
September 7–10. Nineteenth Annual Congress of the United States and Canadian Sections of the International College of Surgeons. Page 828, issue of November 12.
September 12–15. Second International Congress of Cardiology. Page 44, issue of July 2.
September 13–15. American Association of Blood Banks. Notice above.
September 16–18. American Heart Association. Annual Scientific Sessions. Page 44, issue of July 2.
September 22. New England Pediatric Society. Notice above.
October 8 and 9. Academy of Psychosomatic Medicine. Page 748, issue of April 29.
October 27. New England Obstetrical and Gynecological Society. Annual Meeting. Hotel Somerset, Boston.
October 31–November 4. American Institute of Dental Medicine. Notice above.
November 12 and 13. Inter-Society Cytology Council. Notice above.
December 8. New England Pediatric Society. Notice above.
December 13–17. Congress of Obstetrics and Gynecology. Page 748, issue of April 29.
June 21–25, 1955. National Association for the Prevention of Tuberculosis. Page 540, issue of March 25.

CALENDAR FOR THE WEEK BEGINNING THURSDAY, JUNE 10

THURSDAY, JUNE 10

Sixty-Seventh Annual Session of the American Orthopaedic Association. Mount Washington Hotel, Bretton Woods, New Hampshire.
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:00–10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Pediatric Conference. Mount Auburn Hospital, Cambridge.
*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.
*11:00 a.m. Thoracic Conference. Pre- and Postoperative Care of Cardiac Patients. Dr. Harrison Black. Main Amphitheater, Peter Bent Brigham Hospital.
*4:00–5:00 p.m. Pediatric Seminar. Burnham Memorial Hospital (Burnham 4), Massachusetts General Hospital.
5:00 p.m. Case Presentation and Pathological Discussion. Followed by a Subject of Special Presentation. Joslin Amphitheater, New England Deaconess Hospital.

FRIDAY, JUNE 11

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:30–11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–1:00 p.m. Medical Grand Rounds. Dr. Proger and Staff. Stearns Auditorium, New England Center Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.
*4:00–6:00 p.m. X-Ray Conference. Dr. Sosman. Stearns Auditorium, New England Center Hospital.
*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Waltham Street.

SATURDAY, JUNE 12

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Anesthesia Conference. Dr. Etsten. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*9:00 a.m. Proctology Clinic. Peter Bent Brigham Hospital.
*9:00 a.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*9:00–10:30 a.m. Surgical Grand Rounds. Dr. Child and Staff. Stearns Auditorium, New England Center Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*10:30 a.m.–12:00 m. Surgical History Meeting. Stearns Auditorium, New England Center Hospital.
*11:00 a.m.–12:00 m. Hematology Clinic. Dr. William Dameshek, Pratt Auditorium, New England Center Hospital.

MONDAY, JUNE 14

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Medical and Surgical Clinic on Diabetic Foot Problems. New England Deaconess Hospital.

(Notices concluded on page xxi)